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Decreasing COVID-19 In-Hospital Mortality – Lessons from the Pandemic

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Abstract

Introduction: COVID-19 first struck New York City in the spring of 2020 resulting in an unprecedented strain on our health care system triggering multiple changes in public health policy governing hospital operations as well as therapeutic approaches to COVID-19. We examined inpatient mortality at our center throughout the course of the pandemic.

Methods: Retrospective chart review of clinical characteristics, treatments, and outcome data of all patients admitted with COVID-19 from March 1st, 2020 to February 28th, 2021. Patients were grouped into three-month quartiles. Hospital strain was assessed as percent of occupied beds based on a normal bed capacity of 1,491.

Results: Inpatient mortality decreased from 25.0% in spring to 10.8% over the course of the year. During this time, the use of remdesivir, steroids, and anticoagulants increased; the use of hydroxychloroquine and other antibiotics decreased. Daily bed occupation ranged from 62% to 118% and COVID-19 mortality increased by 0.7% per 1% increase in bed occupation (HR 1.007, CI: 1.001, 1.013, p=0.004). In a multivariate model with demographics, comorbidities, acuity of illness, and bed occupation inpatient mortality during the second surge remained significantly lower than during the initial surge (HR 0.520, CI 0.448-0.604, p<0.001). Propensity score analysis confirmed this finding (HR 0.580 CI: 0.507-0.663, p<0.001).

Conclusion: Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in disease specific therapeutics and was associated with bed occupation. Early reduction in epicenter hospital bed occupation to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

Strengths and limitations of this study

- Large cohort study (7,390 COVID-19 patients).
- Longitudinal analysis over 1 year of management and hospital police changes.
- Analysis of mortality changes after adjustment for different therapies and clinical parameters.
- Identification of the association between level of hospital system stress and mortality, with important public health ramifications.
- Limitation: data on most recent variants are not included

Key questions:

What is already known? COVID-19 treatment and mortality changed over one year. Was the percentage of hospital bed occupation associated with in-patient mortality?

What are the new findings? In this retrospective cohort study of 7,390 COVID-19 patients admitted to our institution over a 12-month period, we found that inpatient mortality due to COVID-19 decreased to a degree disproportionate to advances in disease specific therapies. Additionally, inpatient mortality due to COVID-19 was associated with the percentage of hospital bed occupation.

What do the new findings imply? We provide important insights into the temporal changes in COVID-19 prognosis and for the first time identify hospital stress – measured as the percentage of bed occupation – as a parameter independently associated with COVID-19 mortality. Early reductions in epicenter hospital bed occupation to accommodate acutely ill and resource-intensive patients should be critical considerations in the strategic planning for future pandemics.

INTRODUCTION

Coronavirus disease 2019 (COVID-19 was declared a global pandemic by the World Health Organization on March 11th, 2020.[1] In the United States, after a cluster of cases reported from Washington state[2], New York state quickly became the initial epicenter of this pandemic with over 1.27 million of cases till date and over 50,000 fatalities with the highest concentration in the Bronx and Queens boroughs of New York City .[3] Montefiore Einstein, with its three principal teaching hospitals and combined adult bed capacity of 1,491, is the primary health care provider for the large, nearly 1.5 million diverse population of the Bronx[4] and experienced a "first wave" of COVID-19 admissions in the spring of 2020 [3], followed by a significant reduction of cases until a second surge in hospitalizations was noted in the winter of 2020. Throughout the course of the year, multiple public health measures - including those adapting hospital operation to a disaster level pandemic, such as cancellation of all elective procedures and waiver of state specific licensing for health care providers - were put in place. In addition, the understanding of COVID-19 pathophysiology improved [5 6], new treatments were developed [7-10], parts of the general population[11 12] as well as hospital personnel developed antibodies after COVID-19 illness [13], and our hospital system adapted to and then recovered from crisis mode.[14] Here, we report outcomes of patients hospitalized with COVID-19 through one year since the first case, focusing on the differences observed between the spring and the winter surges.

METHODS:

Study Population

We retrospectively reviewed all adult patients admitted to Montefiore Medical Center with a real time reverse transcription polymerase chain reaction (RT-PCR) assay positive for COVID-19

between March 1, 2020 and February 28, 2021. We divided this timeframe in four 3-month seasons: spring (March 1, 2020 to May 31, 2020), summer (June 1, 2020 to August 30, 2020), fall (September 1, 2020 to November 30, 2020), and winter (December 1, 2020 to February 28, 2021).

Data Collection

Medical data including demographic, clinical, and laboratory variables were extracted from the electronic medical record system. The primary outcome was 30-day in-hospital mortality.

Statistical Analysis

Continuous variables are displayed as mean ± standard deviation or median [25-75% interquartile range] and compared with the Student's t-test, or Wilcoxon ranks-sum, as appropriate. Categorical data are presented as percent and compared by the chi-squared test. We estimated the cumulative incidence of the primary endpoint in-hospital mortality for each season, treating hospital discharge as a competing event.[15] To avoid any bias due to differential follow-up length, we censored the follow-up time at 30 days after the admission.

A multivariable competing risk proportional hazard models was used to estimate the sub-distribution hazard ratios[16 17] for time to in-hospital death. Selection method for covariates is presented in the Supplemental Material.

Then we focused on examining the difference in in-hospital death between patients admitted in the spring and in the winter, as they represented the two largest and most temporal distant waves of the COVID-19 pandemic occurring before and after pandemic specific therapeutic hospital

logistic changes had been implemented. Selection method for covariates is presented in the Supplemental Material.

The proportionality assumption was examined [18] and no violation was identified. A two-sided $p<0.05$ was considered statistically significant.

Propensity Score Analysis

To fully control the potential differences in patient population and hospital stress between spring and winter COVID-19 patients, we also used propensity score (PS) matching to compare the 30-day in-hospital mortality between spring and winter admissions. The same covariates used for the multivariable competing risk regression were used for PS matching. PS matching was carried out through a 1:1 greedy matching algorithm, with a caliper width of 0.1 SD. We then stratified on matched pair in the competing risk regression model.[19 20] Because one-to-one matching led to a reduction in sample size, we used this analysis as a sensitivity analysis.

All statistical analyses was performed with SPSS (IBM Corp, ver. 25, Armonk, NY) and the R packages cmprsk and crrSC (R Foundation for Statistical Computing, ver 3.5)

Patient and Public Involvement

Given the retrospective nature of our analysis, it was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

7,390 COVID-19 positive adult patients were admitted between March 1, 2020 and February 28, 2021 (**Figure 1**). 4,495 patients were admitted during the spring, 264 during the summer, 377 during the fall, and 2,254 during the winter.

On April 8, 2020, peak of the spring season, the total numbers of simultaneously adult patients admitted to our hospital (including those admitted to emergency adult wards at our children's hospital[21]) was 1,762 (118% of nominal bed capacity); 1,201 of them (68.2%) were COVID-19 patients. On February 8, 2021, peak of winter season, 1,512 patients (101% of nominal bed capacity) were admitted to our hospital and 393 of them (26.0%) were COVID-19 patients. (**Figure 1**). Following cancellation of elective procedures, bed occupation decreased to 70% by the end of the spring season and remained at 90% until the beginning of the winter season, when the second wave occurred in December 2020. Unadjusted mortality for patient admitted at the beginning of spring, end of spring, beginning of winter, and end of winter was 28%, 8%, 14%, and 13%, respectively (**Figure 2**).

Patient Population

Demographics, past medical history, vital signs at arrivals, and initial laboratory blood tests are presented in **Table 1**. Overall, median age was 66 (55 – 77) years, 3,835 (51.9%) patients were male, 5,519 (74.2%) were of Black race and/or Hispanic ethnicity. Median age ranged from 63 years (fall) to 67 years (spring). Sex distribution was similar throughout the year. Summer and fall patients had the lowest and the highest BMI: 26.7 and 28.6 kg/m^2, respectively.

Pharmacotherapy

Changes in pharmacological approach is presented in **Supplemental Table 1** and **Figure 3**

Spring patients were more likely to receive hydroxychloroquine, azithromycin and other antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2% during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of statins, angiotensin converting inhibitors (ACE-I), or angiotensin receptor blockers (ARBs) also increased.

Death, Intubation, and Length of Stay

Over the course of a year, 1,437 (19.4%) died while hospitalized. Patients who died were older, had more comorbidities, and were more acutely ill consistent within prior reports on risk factors for death in COVID-19[5 6] (**Supplemental Table 2**). Average unadjusted monthly mortality is presented in **Figure 2**. 30-day in-hospital mortality (**Figure 4A**) was 25.0% for the spring patients, 11.0% for summer patients, 6.9% for fall patients, and 11.4% for winter patients ($p<0.001$). On average, spring patients died 6.4 (3.2 – 12.9) days after the arrival to the emergency department, summer patients 7.2 (3.0 – 15.7) days after the arrival, fall patients 13.4 (8.7 – 21.6) days after arrival, and winter patients 13.3 (6.8 – 20.7) days after the arrival ($p<0.001$). Frequency of invasive ventilatory support was higher during the spring with 892 patients (19.4%) intubated, versus 27 (10.2%) in the summer, 36 (9.5%) during fall, and 268 (11.9%) in the winter, $p<0.001$. Median time from arrival-to-intubation was 0.7 (0.1 - 4.1) days for spring patients, 0.6 (0.1 - 8.1) days for summer patients, 2.2 (0.1 – 7.3) days for fall patients, and 2.8 (0.3 – 7.0) days for winter patients, $p<0.001$. Median length of stay was 6.1 (3.5 – 11.1) days during spring, 5.1 (2.7 – 10.1) days during summer, 5.0 (3.0 – 10.1) days during fall, and 6.3 (3.8 – 12.0) days during winter, $p<0.001$.

Bed Saturation and Mortality

In the multivariable competing risk proportional hazard model of the entire cohort, percent of bed occupation was associated with increased 30-day in-hospital mortality (HR 1.007, CI: 1.001, 1.013, p=0.004); i.e mortality increase by 0.7 % for each 1% increase of bed occupation.

Spring vs Winter Mortality Comparison and Propensity Matched Analysis

In the multivariable competing risk proportional hazard model comparing spring and winter season, 30-day in-hospital mortality was lower in winter (HR 0.520, CI 0.448-0.604, p<0.001) when compared to spring. After PS caliper matching, there were 1,722 matched pairs. Spring and winter patients had similar distribution of PS (**Supplemental Figure 1**) and standardized average difference among covariates was greatly reduced. PS analysis showed a significant reduction of in-hospital mortality during winter (HR 0.580 CI: 0.507-0.663, p<0.001) confirming what we observed in the multivariable adjusted analysis (**Figure 4B**).

DISCUSSION

We examined inpatient mortality from COVID-19 over the course of a one-year pandemic at our hospital system in New York City. Our principal findings are as follows: First, we observed a substantial reduction of in-house mortality coinciding with multiple pandemic related public health measures focusing on hospital resources on COVID-19 – and preceding comprehensive changes in pharmacotherapy - towards the end of the first surge. Second, we describe - for the first time - hospital bed occupation as an independent risk factor for inpatient mortality from COVID-19.

Public Health Measures in Response to COVID-19

After declaring a state of disaster emergency (March 7, 2020), New York State introduced different measures to limit the spread of the disease, including public schools closure (March 16, 2020), limitation of indoor dining (March 17, 2020), stay-home order for non-essential workers (March 22, 2020), mandatory face coverings in public (April 15, 2020), and night subway closure (April 30, 2020)[22]. Despite these measures to limit the diffusion of the disease and a generalized reduction of movements around New York City (as evidenced by a more than 90% reduction of subway ridership compared to 2019)[23], more than 30% of Bronx residents were found to have positive antibodies (and thus possibly temporary immunity) against SARS-CoV-2 in August 2020.[24]

Specifically relevant to hospital operations, executive order no. 202.5 (March 16, 2020)[25] allowed healthcare providers not licensed or registered in New York State to temporarily work in the State, and executive order no. 202.10 (March 22, 2020)[25] suspended elective operations. These executive orders were associated with a dramatic drop in non-COVID-19 admissions at our institution beginning March 16, 2020. (**Figure 1**). On March 26, 2020 New York State Governor Cuomo additionally mandated all hospitals to increase their bed capacity by 50% to accommodate the surge of COVID-19 patients.[25] Despite this order, the actual bed occupation at our institution (while accommodating all COVID-19 patients presenting to our hospitals) remained below the usual operating capacity until December 2020.

Notably, COVID-19 mortality remained stable throughout the summer and fall 2020 with low case counts and increased utilization of steroids, anticoagulation, and remdesivir. Although randomized controlled trials have shown morbidity benefits with the use of remdesevir[7] and

mortality reduction with steroids[8], the magnitude of these effects cannot explain the more than 50% reduction in mortality we observed. Furthermore, pharmacotherapy, with the exception of hydroxychloroquine elimination, did not materially change within the spring season, by the end of which mortality was already decreased. Steroid, remdesivir, and therapeutic anticoagulation were used in 10-20% of patients by May 2020, but they reached 30-70% only in the winter season. Despite that, unadjusted mortality began to increase again in December 2020 during the second wave. Of note, bed occupation also increased at that time and proved to be an independent risk factor for COVID-19 mortality in our cohort of nearly 8,000 patients.

Change in Therapeutic Approach

The initial widespread (>2/3 of first spring patients) use of hydroxychloroquine, an agent eventually proven to be ineffective[26] to treat COVID-19, probably represents the most obvious pandemic-associated deviation from the usual multiphase clinical trial standards of therapeutic paradigm development. Only 8 of 2,254 patients received hydroxychloroquine during the winter wave. To a similar extend, we observed a reduction in the use of azithromycin and other antibiotics, the latter possibly reflecting a more careful assessment of the need to treat superimposed bacterial infections during the second wave. Steroid therapy[8 27] and therapeutic anticoagulation[9] were implemented in the majority of patients during the winter after the knowledge on the likely disease modulating inflammatory proprieties and pro-thrombotic effect of COVID-19 had been recognized[28] and, in the case of steroids, a therapeutic effect had been proven[8]. Remdesivir, an inhibitor of the viral RNA-dependent RNA polymerase that showed shortening of recovery time in hospitalized patients with COVID-19 [7], received emergency FDA approval on October 22nd,2020 [29] and was administered to almost half of the admitted patients

during the winter. If initial concerns of possible interactions between ACE-I or ARBs and SARS-CoV-2 [30] led to a possible underutilization or discontinuation of these drugs during the spring, we observed a significant increase in their use during the following months, after no increased risks were reported. [31 32]

Similarly, after several reports showed a possible protective effect associated with the use of statins[33 34], their utilization markedly increased during the winter.

Lastly, after the spring wave provided anecdotal evidence for early proning in COVID-19 pneumonia, an approach strongly favoring noninvasive ventilation and avoiding intubation was developed to address respiratory distress in COVID-19; more data about such an approach has since accumulated. [10 35]

Change in Hospital Stress Load

At the peak of the pandemic, the hospital saturation reached the 118% of the nominal bed capacity and COVID-19 patients accounted for 68.2% of all admitted patients. This increase in acutely ill patients created significant excess demand on the rest of the hospital infrastructure best characterized by the surge in the need for intensive care unit (ICU) beds and transformation of other hospital areas to ICUs.[14 21] Despite increased patient load, the number of standard ICU beds, as well as laboratories, diagnostic equipment, and available personnel, remained the same as before the pandemic. This unmatched patient overload resulted in a 0.7 % mortality increase for each 1% increment in hospital bed saturation.

Limitations

Our study has the shortcomings of a retrospective investigation, but there are some very specific aspects limiting the interpretation of our results. First, it is difficult to assess the true effects of pharmacotherapy given the dynamic changes in indications, doses, and usage that happened over the course of the year. Regardless, we believe the propensity-matched comparison between the spring and the winter waves provides compelling evidence for the validity of our principal observation of inpatient COVID-19 mortality reduction disproportionate to advances in pharmacotherapy. We chose total bed occupation as a metric for hospital stress assuming that other resources per bed remained static. Notably, the ratio of COVID-19 to non-COVID-19 patients, ICU bed saturation, and staff shortages are unaccounted for in this model. Regrettably, an in-depth analysis of these metrics is beyond our ability in this retrospective pandemic analysis with disaster elements. Additionally, a significant number of patients received ICU-level-of-care interventions (mechanical ventilatory support, dialysis, vasopressors titration) on regular floors; therefore, the concept of ICU bed saturation might have been not truly representative of the burden.

However, we feel our data is sufficiently strong to support the notion that bed capacity expansion alone is not the answer. Rather, a smaller number of beds with higher staffing accomplished by drastic reductions in all non-emergent procedures and activities is likely a better approach. Although offering fewer beds in pandemic situation appears initially quite counterintuitive, in practice we observed that mortality began to decrease once beds and resources were allocated specifically to COVID-19 patients by executive orders 202.5 and 202.10; and most importantly that bed occupation never exceeded 100% once hospital operations focused on the COVID-19 pandemic only. Lastly, it is conceivable that an uptrend in mortality observed late in the pandemic with established treatment paradigms could be due to new viral strains or a sicker

patient population. Although we are unable to provide detailed strain analysis for our study population, a meaningful numbers of new (and possibly more virulent) strains were not yet observed in in the Bronx, where our study was conducted.[36] The small sample size of patients in summer and fall does not allow meaningful propensity matched comparisons, and when comparing summer, fall, and winter populations, there do not appear to be clinically meaningful differences.

CONCLUSIONS

Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in disease specific therapeutics and was associated with bed occupation. Early reduction in epicenter hospital bed occupation to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

DECLARATIONS

Ethics approval and consent to participate

The Office of Human Research Affairs at Albert Einstein College of Medicine approved this study (# 2020-11308). Patient consent and HIPAA forms were waived by our IRB due to the retrospective nature of our research.

Consent for publication

Non applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

No conflicts of interest exist.

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Author's Contributions

Design of the project: FC, XX, and UPJ.

Underlying data verified by FC, XX, and UPJ.

Acquisition, analysis, and interpretation of data: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS, and UPJ.

Statistical analysis: FC and XX.

Obtained funding: UPJ

Manuscript writing: FC, XX, and UPJ.

Critical revision of the manuscript for important intellectual content: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS, and UPJ.

Supervision: UPJ

All the Authors reviewed the work and approved the final version.

FC and UPJ had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Demographics, Past Medical History, and Clinical Characteristics of Admitted Patients

	Spring (n=4495)		Summer (n=264)		Fall (n=377)		Winter (n=2254)	
	Sample	**Value**	**Sample**	**Value**	**Sample**	**Value**	**Sample**	**Value**
Demographics								
Age (IQR) - yr	4495	66 (55 - 77)	264	66 (50 - 76)	377	63 (50 - 73)	2254	67 (56 - 77)
Male sex - no (%)	4495	2377 (52.9)	264	138 (52.3)	377	198 (52.5)	2254	1122 (49.8)
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	264	219 (83.0)	377	286 (75.9)	2254	1635 (74.2)
Body Mass Index (IQR) - kg/m^2	4229	28.4 (24.6 - 33)	250	27.6 (22.5 - 32.7)	358	28.6 (25 - 34.1)	2194	28.2 (24.4 - 33.1)
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6)	264	81.7 (76.3 – 85.8)	377	87.6 (83.2 - 90.2)	2254	95.3 (91.9 – 101.8)
Past Medical History								
Hypertension - no (%)	4495	3370 (75)	264	197 (74.6)	377	254 (67.4)	2254	1713 (76)
Sleep apnea - no (%)	4495	521 (11.6)	264	28 (10.6)	377	47 (12.5)	2254	270 (12)
Hyperlipidemia - no (%)	4495	2609 (58)	264	153 (58)	377	199 (52.8)	2254	1380 (61.2)
Atrial fibrillation - no (%)	4495	449 (10)	264	30 (11.4)	377	35 (9.3)	2254	267 (11.8)
Chronic kidney disease - no (%)	4495	1406 (31.3)	264	70 (26.5)	377	85 (22.5)	2254	620 (27.5)
Heart failure - no (%)	4495	980 (21.8)	264	72 (27.3)	377	66 (17.5)	2254	519 (23)
Coronary artery disease - no (%)	4495	1316 (29.3)	264	95 (36)	377	108 (28.6)	2254	721 (32)
Asthma/COPD - no (%)	4495	1371 (30.5)	264	84 (31.8)	377	98 (26)	2254	753 (33.4)
Diabetes mellitus - no (%)	4495	2522 (56.1)	264	148 (56.1)	377	187 (49.6)	2254	1244 (55.2)

Vitals at Presentation								
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	264	98.4 (97.8 - 98.9)	372	98.8 (98.1 - 99.9)	2254	98.7 (98.1 - 99.8)
SBP (IQR) - mmHg	4469	131 (114 - 148)	264	132 (117 - 149)	375	131 (117 - 147)	2254	132 (117 - 148)
DBP (IQR) - mmHg	4465	75 (65 - 84)	263	77 (67 - 87)	374	74 (68 - 84)	2252	75 (67 - 84)
HR (IQR) – bpm	4467	98 (85 - 112)	264	92.5 (76.3 - 105)	372	94 (80 - 107)	2253	95 (82 - 107)
Oxygen saturation (IQR) - %	4463	95 (91 - 98)	264	98 (96 - 99)	372	96 (94 - 98)	2253	96 (92 - 98)
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	264	18 (17 - 20)	372	18 (18 - 20)	2254	19 (18 - 22)
Laboratory Markers								
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	261	12.4 (10.7 - 13.9)	370	13 (11.6 - 14.3)	2228	12.9 (11.5 - 14.2)
Platelet count (IQR) -k/µL	4372	188 (116 - 260)	261	228 (169 - 300)	372	200 (144 - 257)	2228	196 (143 - 259)
White blood cell count (IQR) - k/µL	4372	7.5 (5.6 - 10.6)	261	8 (5.8 - 11)	370	6.6 (5.1 - 8.9)	2228	6.4 (4.7 - 8.8)
Absolute lymphocyte count (IQR) - k/µL	4420	1 (0.7 - 1.4)	263	1.2 (0.9 - 1.8)	374	1.1 (0.8 - 1.5)	2246	1 (0.7 - 1.4)
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	263	138 (135 - 141)	377	137 (135 - 140)	2253	137 (134 - 140)
Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	262	4.2 (3.8 - 4.6)	377	4 (3.8 - 4.4)	2243	4.1 (3.8 - 4.5)
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	263	103 (100 - 105)	377	101 (99 - 104)	2253	101 (98 - 104)
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	263	24 (21 - 27)	377	25 (22 - 27)	2253	24 (21 - 27)
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	263	1 (0.8 - 1.5)	377	1 (0.8 - 1.3)	2253	1.1 (0.8 - 1.5)
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	263	121 (100 - 171)	377	122 (102 - 173)	2253	126 (104 - 184)

Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	245	26 (20 - 38)	354	31 (21 - 47)	2084	35 (24 - 55)
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	252	21 (14 - 32)	361	25 (16 - 41)	2171	26 (17 - 44)
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	220	1.9 (1.4 - 2.7)	330	1.8 (1.3 - 2.5)	1913	1.9 (1.4 - 2.5)
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	160	254.5 (196 - 340)	285	300 (225 - 383)	1563	341 (254 - 468)
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	209	97 (57 - 176)	313	116 (60 - 213)	1957	126 (67 - 282)
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	185	1.1 (0.5 - 2.2)	317	0.8 (0.5 - 1.6)	1907	1.2 (0.7 - 2.3)
Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	120	0.1 (0.1 - 0.4)	254	0.1 (0.1 - 0.2)	1252	0.1 (0.1 - 0.3)
Troponin T* (IQR) - ng/mL	0	NA	219	0.01 (0.01 - 0.03)	342	0.01 (0.01 - 0.02)	2106	0.01 (0.01 - 0.03)
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	3	0.01 (0.01 - 0.01)	0	NA	0	NA
Interleukin-6 (IQR) – pg/mL	1056	33.6 (13.8 - 75.2)	87	11.7 (3 - 43.1)	186	11 (4.7 - 22.2)	710	10.8 (4.3 - 25.6)
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	122	448 (370- 583)	224	540 (436 - 663)	1040	535.5 (434 - 652)
Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	155	228 (90 - 562)	293	364 (166 - 785)	1637	510 (230 - 1094)

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Figure Legends

Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

Figure 2. Cumulative Monthly Admission and Mortality

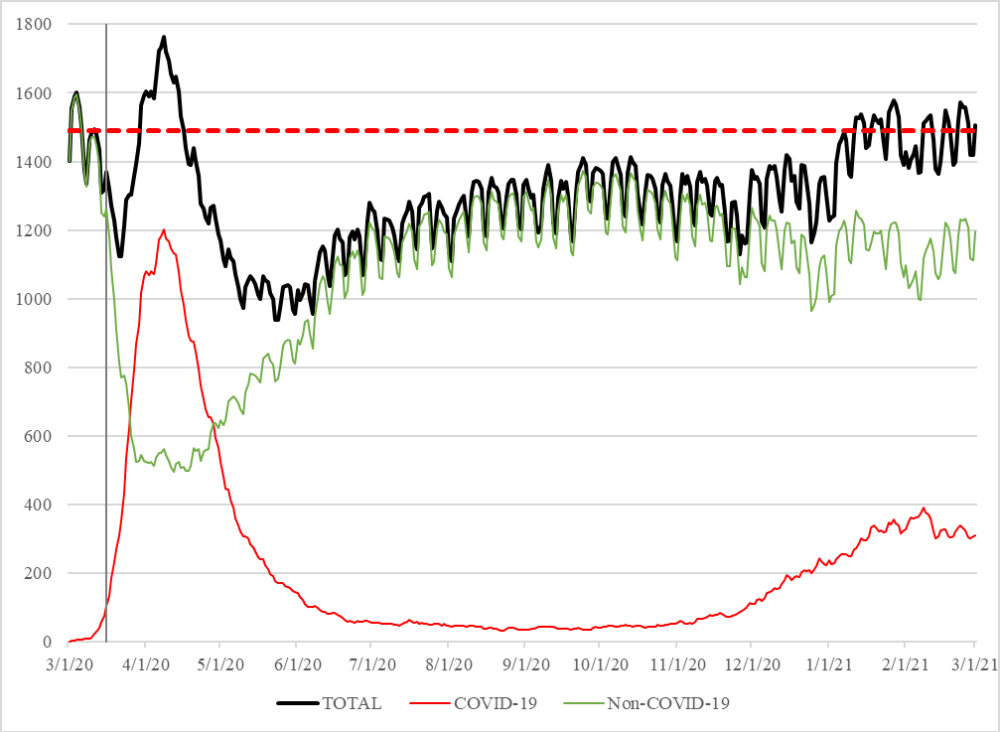
Cumulative monthly admissions (blue line, left axis) and mortality (orange line, right axis) over the year.

Figure 3. Change in Therapies

Percent of patients receiving specific therapies over the year.

Figure 4. Cumulative Incidences

30-day in-hospital mortality by seasons.



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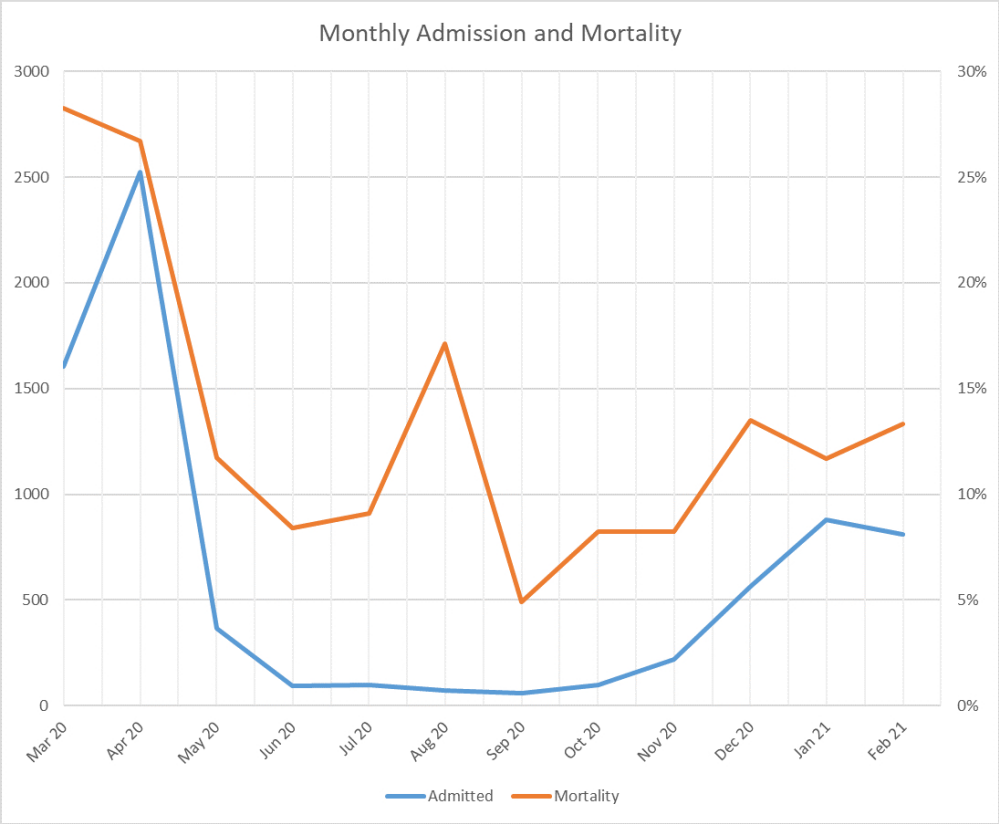

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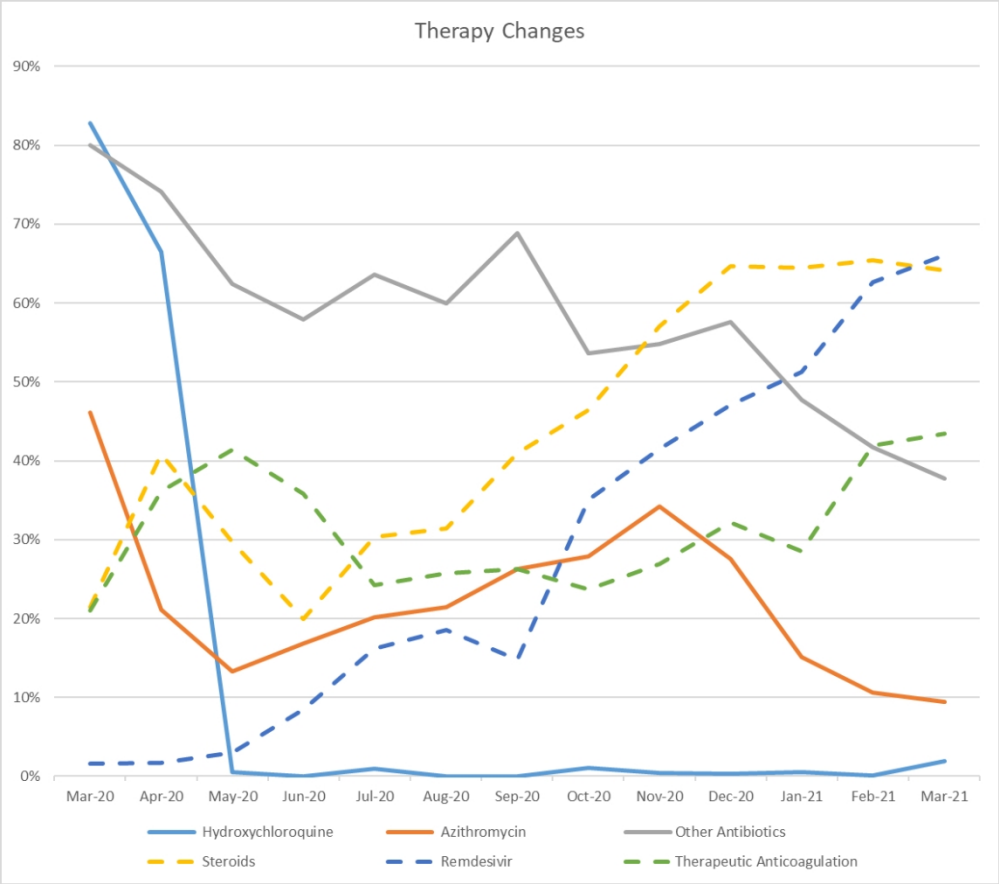

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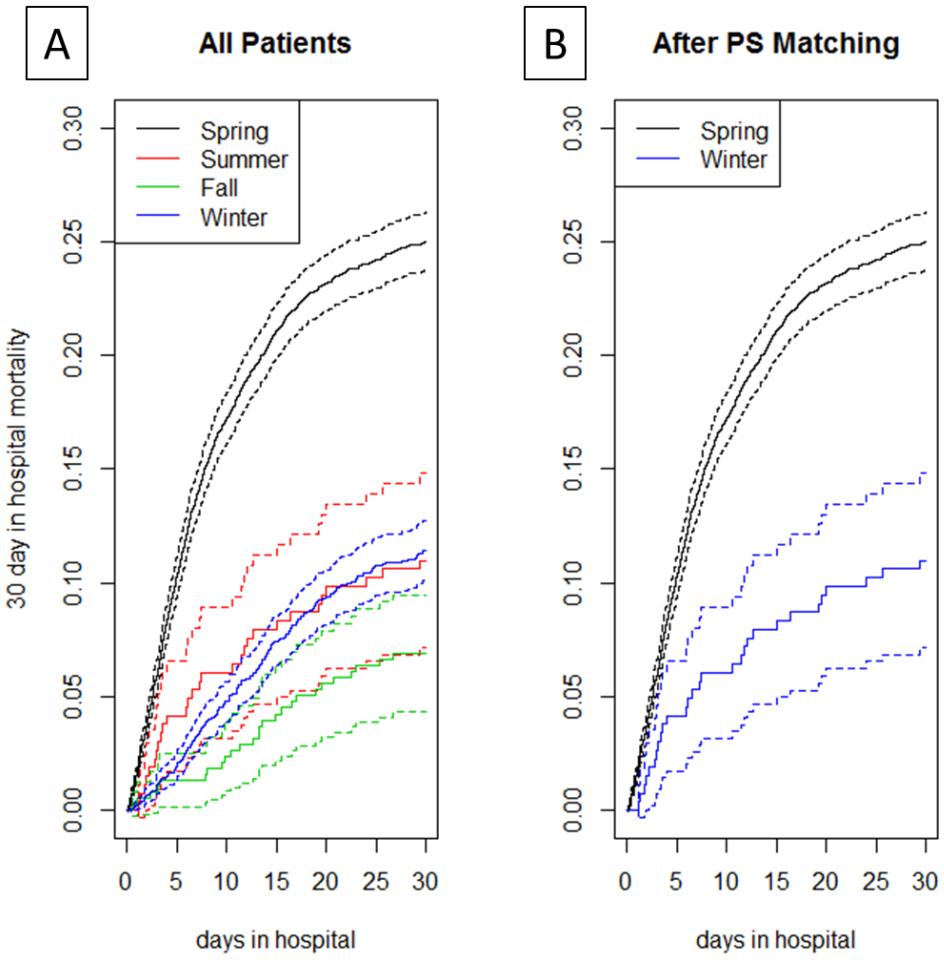

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Supplemental Appendix

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Supplemental Methods

Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for Time to In-hospital Death

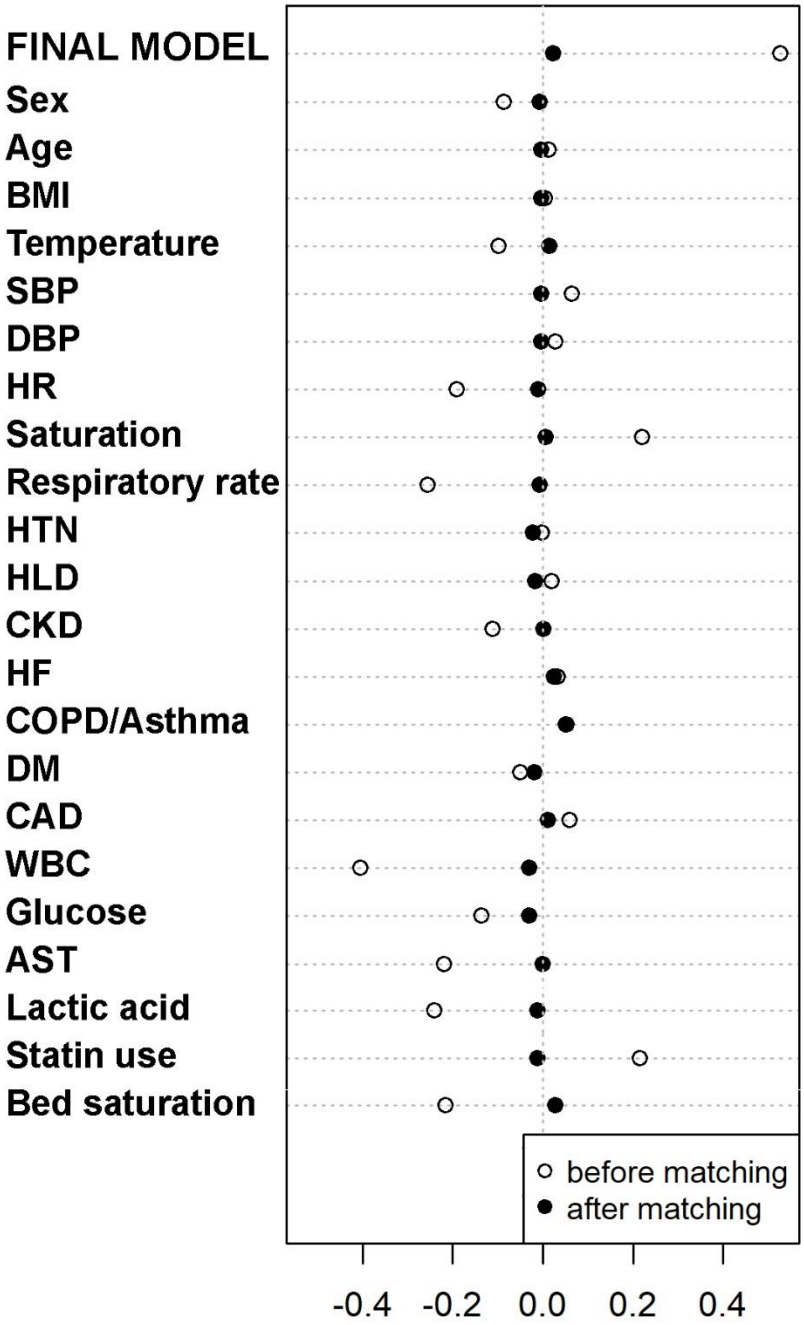
The covariates in the multivariable analyses included factors present in > 90% of our dataset, known to be associated with in-hospital COVID-19 mortality based on prior literature[1-3], or with a univariate association with in-hospital mortality ($p<0.05$) and a clinical (relative difference >5%) difference between survivors and non survivors (**Supplemental Table 2**). These variables included: age, sex, body mass index (BMI), vital signs at presentation (temperature, systolic and diastolic blood pressure, heart rate, respiratory rate, pulse oxygen saturation), platelet count, white cell count, potassium, bicarbonate, creatinine, glucose, alanine transaminase, aspartate transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Additionally, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for in-hospital Death between Patients Spring and Winter Patients

The covariates in the multivariable analyses included factors present in > 90% of our dataset, are known to be associated with in-hospital COVID-19 mortality based on prior literature or with a univariate association between admission season (exposure) or in-hospital mortality (outcome) ($p<0.05$) and a clinical (relative difference >5%) difference between the spring and winter patients (**Supplemental Table 3**). These variables included: age, sex, BMI, vital signs at

presentation, white cell count, creatinine, glucose, alanine transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Also in this model, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

Supplemental Figure 1 - Distribution of Propensity Score



AST = aspartate transaminase; BMI= body mass index; CAD= coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; DBP= diastolic blood pressure; DM = Diabetes mellitus; HF= heart failure; HLD = hyperlipidemia; HNT = hypertension; HR = heart rate; SBP = systolic blood pressure; WBC = white blood cell count

Supplemental Table 1 - Therapies Administered during the Admission

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
Hydroxychloroquine - no (%)	3007 (66.9)	1 (0.4)	2 (0.5)	8 (0.4)
Azithromycin - no (%)	1322 (29.4)	51 (19.3)	118 (31.3)	374 (16.6)
Other antibiotics - no (%)	3382 (75.2)	160 (60.6)	214 (56.8)	1082 (48)
Steroids - no (%)	1485 (33)	71 (26.9)	195 (51.7)	1462 (64.9)
Angiotensin-converting-enzyme Inhibitors - no (%)	318 (7.1)	36 (13.6)	51 (13.5)	269 (11.9)
Angiotensin II receptor blockers - no (%)	264 (5.9)	23 (8.7)	32 (8.5)	212 (9.4)
Statin - no (%)	1478 (32.9)	109 (41.3)	129 (34.2)	1002 (44.5)
Therapeutic anticoagulation - no (%)	1041/4496 (31.2)	76 (28.8)	98 (26.0)	772 (34.3)
Remdesivir* - no (%)	78 (1.7)	37 (14)	134 (35.5)	1224 (54.3)
Lopinavir/Ritonavir – no (%)	40 (0.9)	0 (0)	0 (0)	0 (0)
Ivermectin – no (%)	11 (0.2)	1 (0.4)	0 (0)	34 (1.5)

* 45 patients listed as remdesivir recipients in the spring season were part of a 1:1 double-blind, placebo-controlled study. Instead, all the patients in summer, fall, and winter seasons listed as remdesivir recipients received the actual medication.

Supplemental Table 2 - Comparison Survivors versus Nonsurvivors

	Surviors (n=5953)		Nonsurviors (n=1437)		p-value
	Sample	**Value**	**Sample**	**Value**	
Demographics					
Age (IQR) - yr	5953	64 (52 - 75)	1437	73 (65 - 82)	<0.001
Male sex - no (%)	5953	2989 (50.2)	1437	846 (58.9)	<0.001
Black race and / or Hispanic ethnicity – no (%)	5953	4472 (75.1)	1437	1013 (70.5)	<0.001
Body Mass Index (IQR) - kg/m^2	5679	28.4 (24.6 - 33.2)	1352	27.9 (23.8 - 32.6)	<0.001
Hospital bed saturation (IQR) - %	5953	94.1 (86.5 - 104.8)	1437	99.3 (87.5 - 107.6)	<0.001
Past Medical History					
Hypertension - no (%)	5953	4365 (73.3)	1437	1169 (81.4)	<0.001
Sleep apnea - no (%)	5953	688 (11.6)	1437	178 (12.4)	0.38
Hyperlipidemia - no (%)	5953	3366 (56.5)	1437	975 (67.8)	<0.001
Atrial fibrillation - no (%)	5953	557 (9.4)	1437	224 (15.6)	<0.001
Chronic kidney disease - no (%)	5953	1559 (26.2)	1437	622 (43.3)	<0.001
Heart failure - no (%)	5953	1181 (19.8)	1437	456 (31.7)	<0.001
Coronary artery disease - no (%)	5953	1653 (27.8)	1437	587 (40.8)	<0.001
Asthma/COPD - no (%)	5953	1842 (30.9)	1437	464 (32.3)	0.32
Diabetes mellitus - no (%)	5953	3168 (53.2)	1437	933 (64.9)	<0.001
Vitals at Presentation					
Temperature (IQR) - F	5926	99 (98 - 100)	1427	99 (98 - 100)	0.35

SBP (IQR) - mmHg	5932	132 (117 - 148)	1430	127 (107 - 146)	<0.001
DBP (IQR) - mmHg	5926	76 (67 - 85)	1428	71 (60 - 81)	<0.001
HR (IQR) – bpm	5927	96 (83 - 110)	1429	100 (85 - 114)	<0.001
Oxygen saturation (IQR) - %	5922	96 (93 - 98)	1430	92 (84 - 96)	<0.001
Respiratory Rate (IQR) - bpm	5928	19 (18 - 21)	1428	22 (19 - 26)	<0.001
Laboratory Markers					
Hemoglobin (IQR) - g/dL	5823	12.9 (11.4 - 14.1)	1408	12.6 (10.9 - 14.2)	0.006
Platelet count (IQR) -k/µL	5825	198 (137 - 264)	1408	172 (88 - 246)	<0.001
White blood cell count (IQR) - k/µL	5823	6.9 (5.1 - 9.5)	1408	8.3 (6.0 - 11.9)	<0.001
Absolute lymphocyte count (IQR) - k/µL	5880	1.1 (0.7 - 1.5)	1423	0.9 (0.6 - 1.2)	<0.001
Sodium (IQR) – mEq/L	5879	137 (134 - 140)	1428	138 (134 - 143)	<0.001
Potassium (IQR) – mEq/L	5845	4.2 (3.8 - 4.6)	1426	4.4 (4.0 – 5.0)	<0.001
Chloride (IQR) – mEq/L	5864	100 (96 - 103)	1423	100 (95 - 104)	0.28
Bicarbonates (IQR) – mEq/L	5879	24 (21 - 27)	1428	22 (18 - 25)	<0.001
Creatinine (IQR) - mg/dL	5876	1.0 (0.8 - 1.5)	1427	1.6 (1 - 2.9)	<0.001
Glucose (IQR) - mg/dL	5879	126 (104 - 179)	1428	156 (121 - 236)	<0.001
Aspartate aminotransferase (IQR) - U/L	5416	35 (24 - 55)	1312	52 (33 - 81)	<0.001
Alanine aminotransferase (IQR) - U/L	5614	26 (16 - 42)	1376	28 (18 - 46)	<0.001
Lactic acid (IQR) – mmol/L	5097	1.9 (1.4 - 2.6)	1347	2.6 (1.8 - 3.9)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	4017	384±219	926	518 (371 - 706)	<0.001
Creatine Kinase (IQR) – U/L	4714	336 (253 - 454)	1218	777±2657	<0.001
D-dimer (IQR) - µg/mL	3850	1.2 (0.7 - 2.5)	763	2.5 (1.3 - 6.9)	<0.001
Procalcitonin (IQR) – ng/mL	2800	0.1 (0.1 - 0.3)	615	0.6 (0.2 - 2.4)	<0.001

Troponin T* (IQR) - ng/mL	2365	0.01 (0.01 - 0.03)	302	0.03 (0.01 - 0.1)	<0.001
Troponin I* (IQR) – ng/mL	2684	0.01 (0.01 – 0.02)	981	0.02 (0.01 - 0.08)	<0.001
Interleukin-6 (IQR) – pg/mL	1752	17 (6 - 40)	287	68 (26- 154)	<0.001
Fibrinogen (IQR) – mg/dL	2478	570 (448 - 690)	460	621 (506 - 761)	<0.001
Ferritin (IQR) – ng/mL	3395	521 (224 - 1112)	659	1021 (514 - 2161)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Supplemental Table 3 - Comparison Spring Vs Winter

	Spring (n=4495)		Winter (n=2254)		p-value
	Sample	Value	Sample	Value	
Demographics					
Age (IQR) - yr	4495	66 (55 - 77)	2254	67 (56 - 77)	0.051
Male sex - no (%)	4495	2377 (52.9)	2254	1122 (49.8)	0.016
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	2254	1635 (72.5)	0.098
Body Mass Index (IQR) - kg/m^2	4229	28.4 (24.6 - 33)	2194	28.2 (24.4 - 33.1)	0.433
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6	2254	95.3 (91.9 – 101.8)	<0.001
Past Medical History					
Hypertension - no (%)	4495	3370 (75)	2254	1713 (76)	0.357
Sleep apnea - no (%)	4495	521 (11.6)	2254	270 (12)	0.640
Hyperlipidemia - no (%)	4495	2609 (58)	2254	1380 (61.2)	0.012
Atrial fibrillation - no (%)	4495	449 (10)	2254	267 (11.8)	0.019
Chronic kidney disease - no (%)	4495	1406 (31.3)	2254	620 (27.5)	0.001
Heart failure - no (%)	4495	980 (21.8)	2254	519 (23)	0.254
Coronary artery disease - no (%)	4495	1316 (29.3)	2254	721 (32)	0.022
Asthma/COPD - no (%)	4495	1371 (30.5)	2254	753 (33.4)	0.015
Diabetes mellitus - no (%)	4495	2522 (56.1)	2254	1244 (55.2)	0.475
Vitals at Presentation					
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	2254	98.7 (98.1 - 99.8)	<0.001

SBP (IQR) - mmHg	4469	131 (114 - 148)	2254	132 (117 - 148)	0.002
DBP (IQR) - mmHg	4465	75 (65 - 84)	2252	75 (67 - 84)	0.117
HR (IQR) – bpm	4467	98 (85 - 112)	2253	95 (82 - 107)	<0.001
Oxygen saturation (IQR) - %	4463	95 (91 - 98)	2253	96 (92 - 98)	<0.001
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	2254	19 (18 - 22)	<0.001
Laboratory Markers					
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	2228	12.9 (11.5 - 14.2)	0.030
Platelet count (IQR) -k/µL	4372	188 (116 - 260)	2228	196 (143 - 259)	<0.001
White blood cell count (IQR) - k/µL	4372	7.5 (5.6 - 10.6)	2228	6.4 (4.7 - 8.8)	<0.001
Absolute lymphocyte count (IQR) - k/µL	4420	1 (0.7 - 1.4)	2246	1 (0.7 - 1.4)	0.062
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	2253	137 (134 - 140)	<0.001
Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	2243	4.1 (3.8 - 4.5)	<0.001
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	2253	101 (98 - 104)	<0.001
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	2253	24 (21 - 27)	<0.001
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	2253	1.1 (0.8 - 1.5)	<0.001
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	2253	126 (104 - 184)	<0.001
Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	2084	35 (24 - 55)	<0.001
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	2171	26 (17 - 44)	0.292
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	1913	1.9 (1.4 - 2.5)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	1563	341 (254 - 468)	<0.001
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	1957	126 (67 - 282)	<0.001
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	1907	1.2 (0.7 - 2.3)	<0.001

Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	1252	0.1 (0.1 - 0.3)	<0.001
Troponin T* (IQR) - ng/mL	0	NA	2106	0.01 (0.01 - 0.03)	NA
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	0	NA	NA
Interleukin-6 (IQR) – pg/mL	1056	34 (14 - 75)	710	11 (4 - 26)	<0.001
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	1040	536 (434 - 652)	<0.001
Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	1637	510 (230 - 1094)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Supplemental References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. Jama 2020;323:1239-42.
2. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020;584:430-6.
3. Tartof SY, Qian L, Hong V, et al. Obesity and Mortality Among Patients Diagnosed With COVID-19: Results From an Integrated Health Care Organization. Ann Intern Med 2020;173:773-81.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4-5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 Supp
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12-13
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	Supp
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Impact of COVID-19 Pandemic Management on Outcomes in a Large United States Hospital Center

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Abstract

Introduction: COVID-19 first struck New York City in the spring of 2020 resulting in an unprecedented strain on our health care system triggering multiple changes in public health policy governing hospital operations as well as therapeutic approaches to COVID-19. We examined inpatient mortality at our center throughout the course of the pandemic.

Methods: Retrospective chart review of clinical characteristics, treatments, and outcome data of all patients admitted with COVID-19 from March 1st, 2020 to February 28th, 2021. Patients were grouped into three-month quartiles. Hospital strain was assessed as percent of occupied beds based on a normal bed capacity of 1,491.

Results: Inpatient mortality decreased from 25.0% in spring to 10.8% over the course of the year. During this time, the use of remdesivir, steroids, and anticoagulants increased; the use of hydroxychloroquine and other antibiotics decreased. Daily bed occupancy ranged from 62% to 118% occupancy. In a multivariate model with all year's data controlling for demographics, comorbidities, and acuity of illness, bed occupancy was associated with an increased COVID-19 mortality. Yet further adjustment of bed occupancy showed a significant lower mortality rate during the second surge compared to the initial surge (HR 0.520, CI 0.448-0.604, p<0.001). Propensity score analysis confirmed this difference in these two seasons (HR 0.580 CI: 0.507-0.663, p<0.001).

Conclusion: Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in disease specific therapeutics and was associated with bed occupancy. Early reduction in epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

Strengths and limitations of this study

- Large cohort study (7,390 COVID-19 patients).
- Longitudinal analysis over 1 year of management and hospital policy changes.
- Analysis of mortality changes after adjustment for different therapies and clinical parameters.
- Identification of the association between level of hospital system stress and mortality, with important public health ramifications.
- Limitation: data on most recent variants are not included

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization on March 11th, 2020.[1] In the United States, after a cluster of cases reported from Washington state[2], New York state quickly became the initial epicenter of this pandemic with over 1.27 million of cases till date and over 50,000 fatalities with the highest concentration in the Bronx and Queens boroughs of New York City .[3] Montefiore Einstein, with its three principal teaching hospitals and combined adult bed capacity of 1,491, is the primary health care provider for the large, nearly 1.5 million diverse population of the Bronx[4] and experienced a "first wave" of COVID-19 admissions in the spring of 2020 [3], followed by a significant reduction of cases until a second surge in hospitalizations was noted in the winter of 2020. Throughout the course of the year, multiple public health measures - including those adapting hospital operation to a disaster level pandemic, such as cancellation of all elective procedures and waiver of state specific licensing for health care providers - were put in place. In addition, the understanding of COVID-19 pathophysiology improved [5 6], new treatments were developed [7-10], parts of the general population[11 12] as well as hospital personnel developed antibodies after COVID-19 illness [13], and our hospital system adapted to and then recovered from crisis mode.[14] Here, we report outcomes of patients hospitalized with COVID-19 through one year since the first case, focusing on the differences observed between the spring and the winter surges.

METHODS:

Study Population

We retrospectively reviewed all adult patients admitted to Montefiore Medical Center with a real time reverse transcription polymerase chain reaction (RT-PCR) assay positive for COVID-19

between March 1, 2020 and February 28, 2021. We divided this timeframe in four 3-month seasons based on northern hemisphere calendar: spring (March 1, 2020 to May 31, 2020), summer (June 1, 2020 to August 30, 2020), fall (September 1, 2020 to November 30, 2020), and winter (December 1, 2020 to February 28, 2021).

Data Collection

Medical data including demographic, clinical, and laboratory variables were extracted from the electronic medical record system. The primary outcome was 30-day in-hospital mortality.

Statistical Analysis

Continuous variables are displayed as mean ± standard deviation or median [25-75% interquartile range] and compared with the Student's t-test, or Wilcoxon ranks-sum, as appropriate. Categorical data are presented as percent and compared by the chi-squared test. We estimated the cumulative incidence of the primary endpoint in-hospital mortality for each season, treating hospital discharge as a competing event.[15] To avoid any bias due to differential follow-up length, we censored the follow-up time at 30 days after the admission.

A multivariable competing risk proportional hazard models was used to estimate the sub-distribution hazard ratios[16 17] for time to in-hospital death. The covariates in the multivariable analyses included factors present in > 90% of our dataset, known to be associated with in-hospital COVID-19 mortality based on prior literature[6 18 19], or with a univariate association with in-hospital mortality ($p<0.05$) and a clinical (relative difference >5%) difference between survivors and non survivors (**Supplemental Table 1**). These variables included: age, sex, body mass index (BMI), vital signs at presentation (temperature, systolic and diastolic blood pressure,

heart rate, respiratory rate, pulse oxygen saturation), platelet count, white cell count, potassium, bicarbonate, creatinine, glucose, alanine transaminase, aspartate transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Additionally, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

Then we focused on examining the difference in in-hospital death between patients admitted in the spring and in the winter, as they represented the two largest and most temporal distant waves of the COVID-19 pandemic occurring before and after public health polices, specific therapeutic approaches and hospital management changes had been implemented. Selection method for covariates is presented in the **Supplemental Material** and **Supplemental Table 2**.

The proportionality assumption was examined [20] and no violation was identified. A two-sided $p<0.05$ was considered statistically significant.

Propensity Score Analysis

To fully control the potential differences in patient population and hospital stress between spring and winter COVID-19 patients, we also used propensity score (PS) matching to compare the 30-day in-hospital mortality between spring and winter admissions. The same covariates used for the multivariable competing risk regression were used for PS matching. PS matching was carried out through a 1:1 greedy matching algorithm, with a caliper width of 0.1 SD. We then stratified on matched pair in the competing risk regression model.[21 22] Because one-to-one matching led to a reduction in sample size, we used this analysis as a sensitivity analysis.

All statistical analyses was performed with SPSS (IBM Corp, ver. 25, Armonk, NY) and the R packages cmprsk and crrSC (R Foundation for Statistical Computing, ver 3.5)

Patient and Public Involvement

Given the retrospective nature of our analysis, it was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

7,390 COVID-19 positive adult patients were admitted between March 1, 2020 and February 28, 2021 (**Figure 1**). 4,495 patients were admitted during the spring, 264 during the summer, 377 during the fall, and 2,254 during the winter.

On April 8, 2020, peak of the spring season, the total numbers of simultaneously adult patients admitted to our hospital (including those admitted to emergency adult wards at our children's hospital[23]) was 1,762 (118% of nominal bed capacity); 1,201 of them (68.2%) were COVID-19 patients. On February 8, 2021, peak of winter season, 1,512 patients (101% of nominal bed capacity) were admitted to our hospital and 393 of them (26.0%) were COVID-19 patients. (**Figure 1**). Following cancellation of elective procedures, bed occupancy decreased to 70% by the end of the spring season and remained at 90% until the beginning of the winter season, when the second wave occurred in December 2020. Unadjusted mortality for patient admitted at the beginning of spring, end of spring, beginning of winter, and end of winter was 28%, 8%, 14%, and 13%, respectively (**Figure 2**).

Patient Population

Demographics, past medical history, vital signs at arrivals, and initial laboratory blood tests are presented in **Table 1**. Overall, median age was 66 (55 – 77) years, 3,835 (51.9%) patients were male, 5,519 (74.2%) were of Black race and/or Hispanic ethnicity. Median age ranged from 63 years (fall) to 67 years (spring). Sex distribution was similar throughout the year. Summer and fall patients had the lowest and the highest BMI: 26.7 and 28.6 kg/m^2, respectively.

Pharmacotherapy

Changes in pharmacological approach is presented in **Supplemental Table 3** and **Figure 3.** Spring patients were more likely to receive hydroxychloroquine, azithromycin and other antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2% during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of statins, angiotensin converting inhibitors (ACE-I), or angiotensin receptor blockers (ARBs) also increased.

Death, Intubation, and Length of Stay

Over the course of a year, 1,437 (19.4%) died while hospitalized. Patients who died were older, had more comorbidities, and were more acutely ill consistent within prior reports on risk factors for death in COVID-19[5 6] (**Supplemental Table 1**). Average unadjusted monthly mortality is presented in **Figure 2**. 30-day in-hospital mortality (**Figure 4A**) was 25.0% for the spring patients, 11.0% for summer patients, 6.9% for fall patients, and 11.4% for winter patients ($p<0.001$). On average, spring patients died 6.4 (3.2 – 12.9) days after the arrival to the

emergency department, summer patients 7.2 (3.0 – 15.7) days after the arrival, fall patients 13.4 (8.7 – 21.6) days after arrival, and winter patients 13.3 (6.8 – 20.7) days after the arrival ($p<0.001$). Frequency of invasive ventilatory support was higher during the spring with 892 patients (19.4%) intubated, versus 27 (10.2%) in the summer, 36 (9.5%) during fall, and 268 (11.9%) in the winter, $p<0.001$. Median time from arrival-to-intubation was 0.7 (0.1 - 4.1) days for spring patients, 0.6 (0.1 - 8.1) days for summer patients, 2.2 (0.1 – 7.3) days for fall patients, and 2.8 (0.3 – 7.0) days for winter patients, $p<0.001$. Median length of stay was 6.1 (3.5 – 11.1) days during spring, 5.1 (2.7 – 10.1) days during summer, 5.0 (3.0 – 10.1) days during fall, and 6.3 (3.8 – 12.0) days during winter, $p<0.001$.

Bed Saturation and Mortality

We defined bed saturation the percentage of bed occupancy calculated from the ratio between the number of admitted patients over the nominal bed capacity of our institution (1,491).

In the multivariable competing risk proportional hazard model of the entire cohort, percent of bed occupancy was associated with increased 30-day in-hospital mortality (HR 1.007, CI: 1.001, 1.013, $p=0.004$); i.e mortality increase by 0.7 % for each 1% increase of bed occupancy. Consistent results were observed per level increase in bed occupancy quartile, (HR 1.086 [1.026 -1.148], P-value for linear trend = 0.004). Results of the competing risk regression analysis are presented in the **Table 2.**

Spring vs Winter Mortality Comparison and Propensity Matched Analysis

In the multivariable competing risk proportional hazard model comparing spring and winter season, 30-day in-hospital mortality was lower in winter (HR 0.520, CI 0.448-0.604, $p<0.001$)

when compared to spring. After PS caliper matching, there were 1,722 matched pairs. Spring and winter patients had similar distribution of PS (**Supplemental Figure 1**) and standardized average difference among covariates was greatly reduced. PS analysis showed a significant reduction of in-hospital mortality during winter (HR 0.580 CI: 0.507-0.663, p<0.001) confirming what we observed in the multivariable adjusted analysis (**Figure 4B**).

DISCUSSION

We examined inpatient mortality from COVID-19 over the course of a one-year pandemic at our hospital system in New York City. Our principal findings are as follows: First, we observed a substantial reduction of in-hospital mortality coinciding with multiple pandemic related public health measures focusing on hospital resources on COVID-19 – and preceding comprehensive changes in pharmacotherapy - towards the end of the first surge. Second, we describe - for the first time - hospital bed occupancy as an independent risk factor for inpatient mortality from COVID-19.

Public Health Measures in Response to COVID-19

After declaring a state of disaster emergency (March 7, 2020), New York State introduced different measures to limit the spread of the disease, including public schools closure (March 16, 2020), limitation of indoor dining (March 17, 2020), stay-home order for non-essential workers (March 22, 2020), mandatory face coverings in public (April 15, 2020), and night subway closure (April 30, 2020)[24]. Despite these measures to limit the diffusion of the disease and a generalized reduction of movements around New York City (as evidenced by a more than 90% reduction of subway ridership compared to 2019)[25], more than 30% of Bronx residents were

found to have positive antibodies (and thus possibly temporary immunity) against SARS-CoV-2 in August 2020.[26]

Specifically relevant to hospital operations, executive order no. 202.5 (March 16, 2020)[27] allowed healthcare providers not licensed or registered in New York State to temporarily work in the State, and executive order no. 202.10 (March 22, 2020)[27] suspended elective operations. These executive orders were associated with a dramatic drop in non-COVID-19 admissions at our institution beginning March 16, 2020. (**Figure 1**). On March 26, 2020 New York State Governor Cuomo additionally mandated all hospitals to increase their bed capacity by 50% to accommodate the surge of COVID-19 patients.[27] Despite this order, the actual bed occupancy at our institution (while accommodating all COVID-19 patients presenting to our hospitals) remained below the usual operating capacity until December 2020.

Notably, COVID-19 mortality remained stable throughout the summer and fall 2020 with low case counts and increased utilization of steroids, anticoagulation, and remdesivir. Although randomized controlled trials have shown morbidity benefits with the use of remdesevir[7] and mortality reduction with steroids[8], the magnitude of these effects cannot explain the more than 50% reduction in mortality we observed. Furthermore, pharmacotherapy, with the exception of hydroxychloroquine elimination, did not materially change within the spring season, by the end of which mortality was already decreased. Steroid, remdesivir, and therapeutic anticoagulation were used in 10-20% of patients by May 2020, but they reached 30-70% only in the winter season. Despite that, unadjusted mortality began to increase again in December 2020 during the second wave. Of note, bed occupancy also increased at that time and proved to be an independent risk factor for COVID-19 mortality in our cohort of nearly 8,000 patients.

Change in Therapeutic Approach

The initial widespread (>2/3 of first spring patients) use of hydroxychloroquine, an agent eventually proven to be ineffective[28] to treat COVID-19, probably represents the most obvious pandemic-associated deviation from the usual multiphase clinical trial standards of therapeutic paradigm development. Only 8 of 2,254 patients received hydroxychloroquine during the winter wave. Similarly, we observed a reduction in the use of azithromycin and other antibiotics, the latter possibly reflecting a more careful assessment of the need to treat superimposed bacterial infections during the second wave. Steroid therapy[8 29] and therapeutic anticoagulation[9] were implemented in the majority of patients during the winter after the knowledge on the likely disease modulating inflammatory proprieties and pro-thrombotic effect of COVID-19 had been recognized[30] and, in the case of steroids, a therapeutic effect had been proven[8]. Remdesivir, an inhibitor of the viral RNA-dependent RNA polymerase that showed shortening of recovery time in hospitalized patients with COVID-19 [7], received emergency FDA approval on October 22nd,2020 [31] and was administered to almost half of the admitted patients during the winter. If initial concerns of possible interactions between ACE-I or ARBs and SARS-CoV-2 [32] led to a possible underutilization or discontinuation of these drugs during the spring, we observed a significant increase in their use during the following months, after no increased risks were reported. [33 34]

Similarly, after several reports showed a possible protective effect associated with the use of statins[35 36], their utilization markedly increased during the winter.

Lastly, after the spring wave provided anecdotal evidence for early proning in COVID-19 pneumonia, an approach strongly favoring noninvasive ventilation and avoiding intubation was developed to address respiratory distress in COVID-19; more data about such an approach has

since accumulated. [10 37] The cumulative effect of these therapeutic changes, in combination with a better preparedness to respond to a pandemic, can be estimate from the different mortality between the first surge (spring) and the second surge (winter). After matching the two groups for demographic and clinical variables, as well as for elements indicative of hospital distress (bed occupancy), a significant reduction of mortality was observed during the winter trimester.

Change in Hospital Stress Load

At the peak of the pandemic, the hospital saturation reached the 118% of the nominal bed capacity and COVID-19 patients accounted for 68.2% of all admitted patients. This increase in acutely ill patients created significant excess demand on the rest of the hospital infrastructure best characterized by the surge in the need for intensive care unit (ICU) beds and transformation of other hospital areas to ICUs.[14 23] Despite increased patient load, the number of standard ICU beds, as well as laboratories, diagnostic equipment, and available personnel, remained the same as before the pandemic. This unmatched patient overload resulted in a 0.7 % mortality increase for each 1% increment in hospital bed saturation. In light of these results, strategies to minimize the bed occupancy for non-Covid-19 patients or non-life-saving admission should be adopted to diverge resources to improve the outcome of admitted Covid-19 patients.

Limitations

Our study has the shortcomings of a retrospective investigation, but there are some very specific aspects limiting the interpretation of our results. First, it is difficult to assess the true effects of pharmacotherapy given the dynamic changes in indications, doses, and usage that happened over the course of the year. Regardless, we believe the propensity-matched comparison between the

spring and the winter waves provides compelling evidence for the validity of our principal observation of inpatient COVID-19 mortality reduction disproportionate to advances in pharmacotherapy. We chose total bed occupancy as a metric for hospital stress assuming that other resources per bed remained static. Notably, the ratio of COVID-19 to non-COVID-19 patients, ICU bed saturation, and staff shortages are unaccounted for in this model. Regrettably, an in-depth analysis of these metrics is beyond our ability in this retrospective pandemic analysis with disaster elements. Additionally, a significant number of patients received ICU-level-of-care interventions (mechanical ventilatory support, dialysis, vasopressors titration) on regular floors; therefore, the concept of ICU bed saturation might have been not truly representative of the burden.

However, we feel our data is sufficiently strong to support the notion that bed capacity expansion alone is not the answer. Rather, a smaller number of beds with higher staffing accomplished by drastic reductions in all non-emergent procedures and activities is likely a better approach. Although offering fewer beds in pandemic situation appears initially quite counterintuitive, in practice we observed that mortality began to decrease once beds and resources were allocated specifically to COVID-19 patients by executive orders 202.5 and 202.10; and most importantly that bed occupancy never exceeded 100% once hospital operations focused on the COVID-19 pandemic only.It is conceivable that an uptrend in mortality observed late in the pandemic with established treatment paradigms could be due to new viral strains or a sicker patient population. Although we are unable to provide detailed strain analysis for our study population, a meaningful numbers of new (and possibly more virulent) strains were not yet observed in in the Bronx, where our study was conducted.[38] The small sample size of patients in summer and fall does not allow meaningful propensity matched comparisons, and when comparing summer, fall, and

winter populations, there do not appear to be clinically meaningful differences. Lastly, single-patient data on vaccination status were not available. At the conclusion of the study, only 13.8% of the population of New York State received at least one dose and 7.4% received two doses[39]. Given the heterogeneous distribution of vaccination within the state (and the city of New York), it is impossible to meaningfully account for these parameters.

CONCLUSIONS

Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in disease specific therapeutics and was associated with bed occupancy. Early reduction in epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

DECLARATIONS

Ethics approval and consent to participate

The Office of Human Research Affairs at Albert Einstein College of Medicine approved this study (# 2020-11308). Patient consent and HIPAA forms were waived by our IRB due to the retrospective nature of our research.

Consent for publication

Non applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

No conflicts of interest exist.

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Author's Contributions

Design of the project: FC, XX, and UPJ.

Underlying data verified by FC, XX, and UPJ.

Acquisition, analysis, and interpretation of data: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS, and UPJ.

Statistical analysis: FC and XX.

Obtained funding: UPJ

Manuscript writing: FC, XX, and UPJ.

Critical revision of the manuscript for important intellectual content: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS, and UPJ.

Supervision: UPJ

All the Authors reviewed the work and approved the final version.

FC and UPJ had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Demographics, Past Medical History, and Clinical Characteristics of Admitted Patients

	Spring (n=4495)		Summer (n=264)		Fall (n=377)		Winter (n=2254)	
	Sample	**Value**	**Sample**	**Value**	**Sample**	**Value**	**Sample**	**Value**
30-Day hospital outcome								
Still admitted - no (%)	4495	194 (4.3)	264	6 (2.3)	377	15 (4.0)	2254	103 (4.6)
Discharged alive - no (%)	4495	3177 (70.7)	264	229 (86.7)	377	336 (89.1)	2254	1893 (84.0)
Dead in the hospital - no (%)	4495	1124 (25.0)	264	29 (11.0)	377	26 (6.9)	2254	258 (11.4)
Demographics								
Age (IQR) - yr	4495	66 (55 - 77)	264	66 (50 - 76)	377	63 (50 - 73)	2254	67 (56 - 77)
Male sex - no (%)	4495	2377 (52.9)	264	138 (52.3)	377	198 (52.5)	2254	1122 (49.8)
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	264	219 (83.0)	377	286 (75.9)	2254	1635 (74.2)
Body Mass Index (IQR) - kg/m^2	4229	28.4 (24.6 - 33)	250	27.6 (22.5 - 32.7)	358	28.6 (25 - 34.1)	2194	28.2 (24.4 - 33.1)
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6)	264	81.7 (76.3 – 85.8)	377	87.6 (83.2 - 90.2)	2254	95.3 (91.9 – 101.8)
Past Medical History								
Hypertension - no (%)	4495	3370 (75)	264	197 (74.6)	377	254 (67.4)	2254	1713 (76)
Sleep apnea - no (%)	4495	521 (11.6)	264	28 (10.6)	377	47 (12.5)	2254	270 (12)
Hyperlipidemia - no (%)	4495	2609 (58)	264	153 (58)	377	199 (52.8)	2254	1380 (61.2)
Atrial fibrillation - no (%)	4495	449 (10)	264	30 (11.4)	377	35 (9.3)	2254	267 (11.8)

Chronic kidney disease - no (%)	4495	1406 (31.3)	264	70 (26.5)	377	85 (22.5)	2254	620 (27.5)
Heart failure - no (%)	4495	980 (21.8)	264	72 (27.3)	377	66 (17.5)	2254	519 (23)
Coronary artery disease - no (%)	4495	1316 (29.3)	264	95 (36)	377	108 (28.6)	2254	721 (32)
Asthma/COPD - no (%)	4495	1371 (30.5)	264	84 (31.8)	377	98 (26)	2254	753 (33.4)
Diabetes mellitus - no (%)	4495	2522 (56.1)	264	148 (56.1)	377	187 (49.6)	2254	1244 (55.2)
Vitals at Presentation								
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	264	98.4 (97.8 - 98.9)	372	98.8 (98.1 - 99.9)	2254	98.7 (98.1 - 99.8)
SBP (IQR) - mmHg	4469	131 (114 - 148)	264	132 (117 - 149)	375	131 (117 - 147)	2254	132 (117 - 148)
DBP (IQR) - mmHg	4465	75 (65 - 84)	263	77 (67 - 87)	374	74 (68 - 84)	2252	75 (67 - 84)
HR (IQR) – bpm	4467	98 (85 - 112)	264	92.5 (76.3 - 105)	372	94 (80 - 107)	2253	95 (82 - 107)
Oxygen saturation (IQR) - %	4463	95 (91 - 98)	264	98 (96 - 99)	372	96 (94 - 98)	2253	96 (92 - 98)
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	264	18 (17 - 20)	372	18 (18 - 20)	2254	19 (18 - 22)
Laboratory Markers								
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	261	12.4 (10.7 - 13.9)	370	13 (11.6 - 14.3)	2228	12.9 (11.5 - 14.2)
Platelet count (IQR) -k/µL	4372	188 (116 - 260)	261	228 (169 - 300)	372	200 (144 - 257)	2228	196 (143 - 259)
White blood cell count (IQR) - k/µL	4372	7.5 (5.6 - 10.6)	261	8 (5.8 - 11)	370	6.6 (5.1 - 8.9)	2228	6.4 (4.7 - 8.8)
Absolute lymphocyte count (IQR) - k/µL	4420	1 (0.7 - 1.4)	263	1.2 (0.9 - 1.8)	374	1.1 (0.8 - 1.5)	2246	1 (0.7 - 1.4)
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	263	138 (135 - 141)	377	137 (135 - 140)	2253	137 (134 - 140)

Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	262	4.2 (3.8 - 4.6)	377	4 (3.8 - 4.4)	2243	4.1 (3.8 - 4.5)
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	263	103 (100 - 105)	377	101 (99 - 104)	2253	101 (98 - 104)
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	263	24 (21 - 27)	377	25 (22 - 27)	2253	24 (21 - 27)
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	263	1 (0.8 - 1.5)	377	1 (0.8 - 1.3)	2253	1.1 (0.8 - 1.5)
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	263	121 (100 - 171)	377	122 (102 - 173)	2253	126 (104 - 184)
Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	245	26 (20 - 38)	354	31 (21 - 47)	2084	35 (24 - 55)
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	252	21 (14 - 32)	361	25 (16 - 41)	2171	26 (17 - 44)
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	220	1.9 (1.4 - 2.7)	330	1.8 (1.3 - 2.5)	1913	1.9 (1.4 - 2.5)
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	160	254.5 (196 - 340)	285	300 (225 - 383)	1563	341 (254 - 468)
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	209	97 (57 - 176)	313	116 (60 - 213)	1957	126 (67 - 282)
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	185	1.1 (0.5 - 2.2)	317	0.8 (0.5 - 1.6)	1907	1.2 (0.7 - 2.3)
Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	120	0.1 (0.1 - 0.4)	254	0.1 (0.1 - 0.2)	1252	0.1 (0.1 - 0.3)
Troponin T* (IQR) - ng/mL	0	NA	219	0.01 (0.01 - 0.03)	342	0.01 (0.01 - 0.02)	2106	0.01 (0.01 - 0.03)
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	3	0.01 (0.01 - 0.01)	0	NA	0	NA
Interleukin-6 (IQR) – pg/mL	1056	33.6 (13.8 - 75.2)	87	11.7 (3 - 43.1)	186	11 (4.7 - 22.2)	710	10.8 (4.3 - 25.6)
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	122	448 (370- 583)	224	540 (436 - 663)	1040	535.5 (434 - 652)

Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	155	228 (90 - 562)	293	364 (166 - 785)	1637	510 (230 - 1094)

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Table 2. Association with In-Hospital Mortality (Regression models with competing risks)

	Multivariable	
Variable	**HR (95% CI)**	**P-value**
Age - yr	1.046 (1.04 - 1.051)	<0.001
Male sex - yes/no	1.352 (1.187 - 1.54)	<0.001
Body mass index - kg/m2	1.022 (1.012 - 1.032)	<0.001
Temperature - F	1.071 (1.036 - 1.108)	<0.001
SBP - mmHg	0.994 (0.991 - 0.997)	<0.001
DBP - mmHg	0.996 (0.991 - 1.001)	0.14
HR - bpm	1.003 (0.999 - 1.006)	0.11
Oxygen saturation - %	0.967 (0.961 - 0.972)	<0.001
Respiratory rate - bpm	1.027 (1.019 - 1.035)	<0.001
White blood cell count - k/µL	1.008 (1.001 - 1.016)	0.02
Glucose - mg/dL	1.001 (1 - 1.001)	0.001
Aspartate aminotransferase - U/L	1 (1 - 1.001)	0.21
Alanine aminotransferase - U/L	1 (0.999 - 1)	0.25
Lactic acid – mmol/L	1.071 (1.036 - 1.107)	<0.001
Platelet count -k/µL	0.999 (0.998 - 0.999)	<0.001
Potassium – mEq/L	1.096 (1.028 - 1.168)	0.0052
Bicarbonates – mEq/L	0.957 (0.944 - 0.971)	<0.001
Creatinine - mg/dL	1.023 (0.998 - 1.049)	0.069
HTN - yes/no	1.008 (0.851 - 1.194)	0.93
HLD - yes/no	1.196 (1.02 - 1.401)	0.027
CKD - yes/no	1.263 (1.09 - 1.462)	0.002
HF - yes/no	1.33 (1.146 - 1.543)	<0.001
COPD/Asthma - yes/no	0.948 (0.827 - 1.088)	0.45
DM - yes/no	0.946 (0.819 - 1.093)	0.45
CAD - yes/no	1.101 (0.955 - 1.271)	0.19
Statin use - %	0.577 (0.501 - 0.664)	<0.001
Bed occupancy - %	1.007 (1.002 - 1.013)	0.004

CAD = Coronary artery disease; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; DM= Diabetes mellitus; HLD = hyperlipidemia; HF = Heart failure; HR = Heart rate; HTN = Hypertension; SBP = Systolic blood pressure

Figure Legends

Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

Figure 2. Cumulative Monthly Admission and Mortality

Cumulative monthly admissions (blue line, left axis) and mortality (orange line, right axis) over the year.

Figure 3. Change in Therapies

Percent of patients receiving specific therapies over the year.

Figure 4. Cumulative Incidences

30-day in-hospital mortality by seasons.

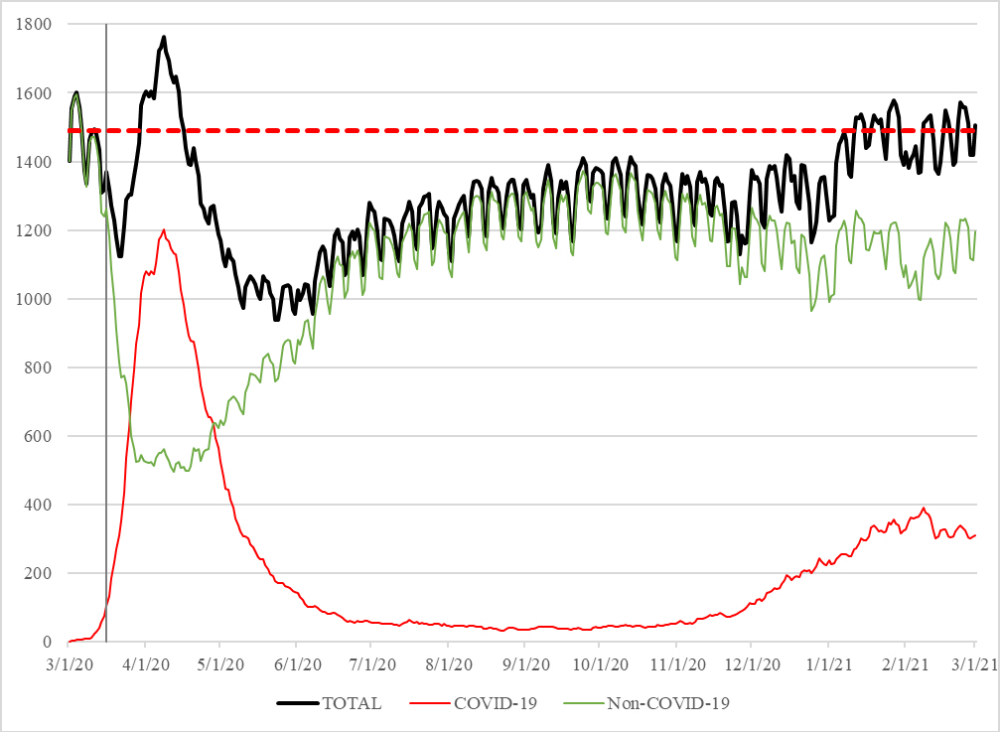

Figure 1

85x62mm (300 x 300 DPI)

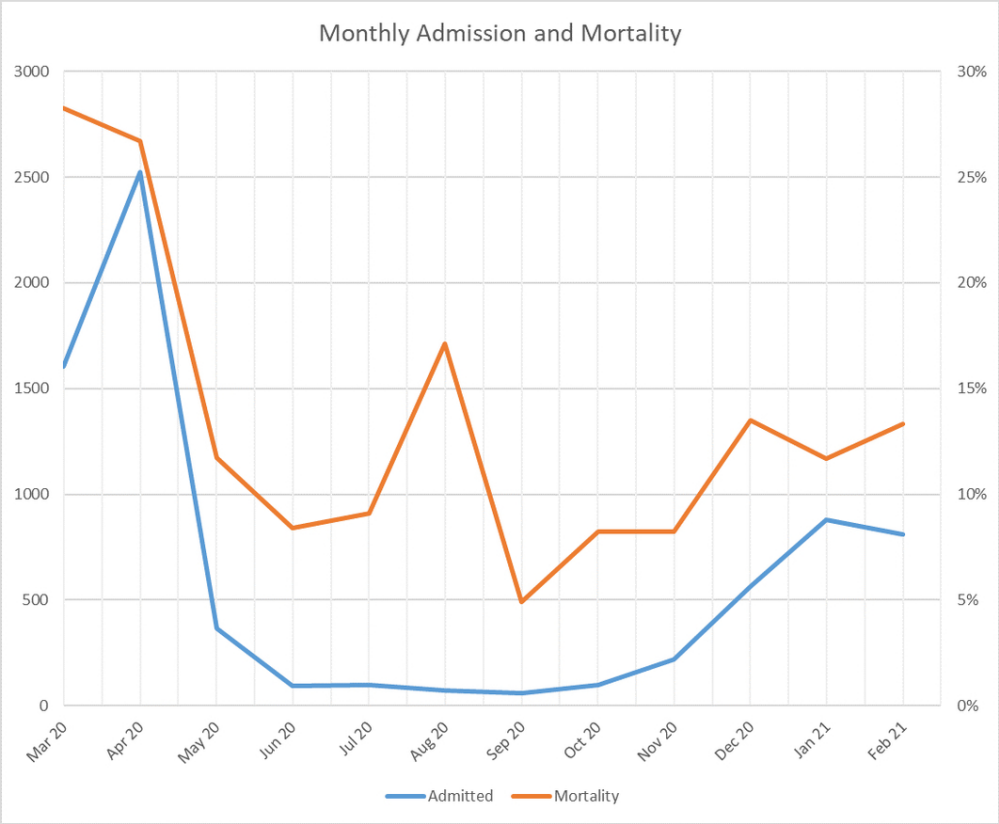

Figure 2

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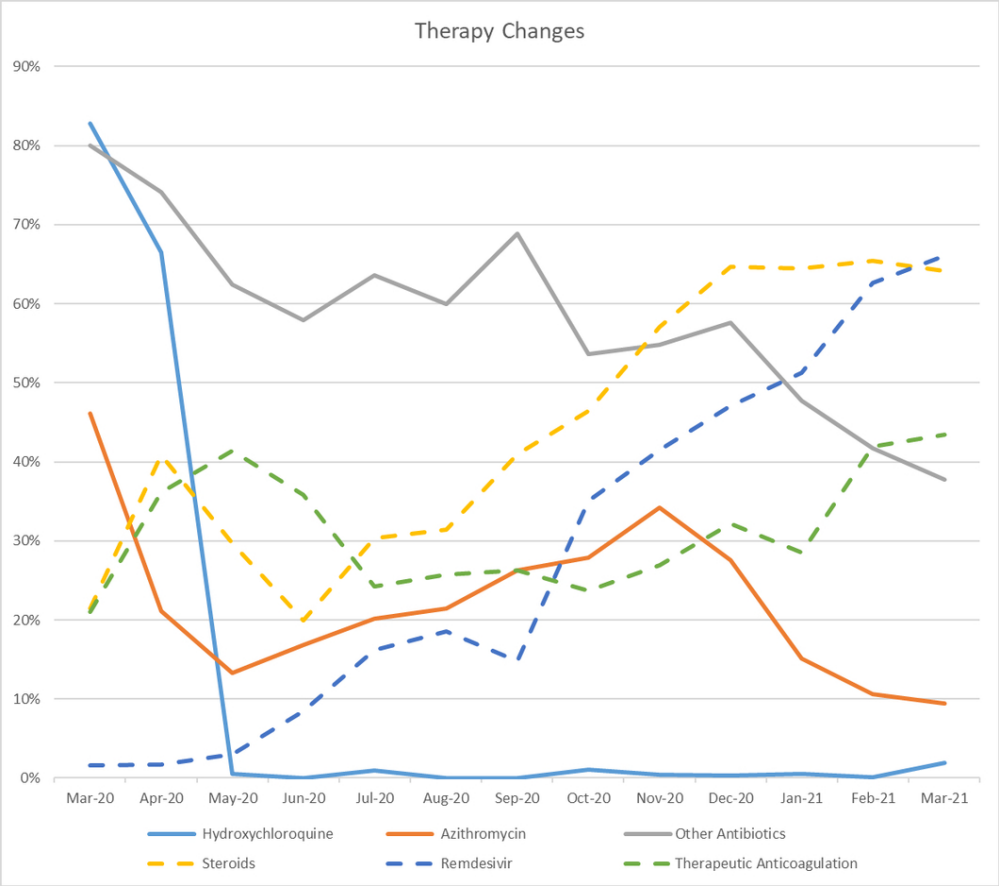

Figure 3

89x79mm (300 x 300 DPI)

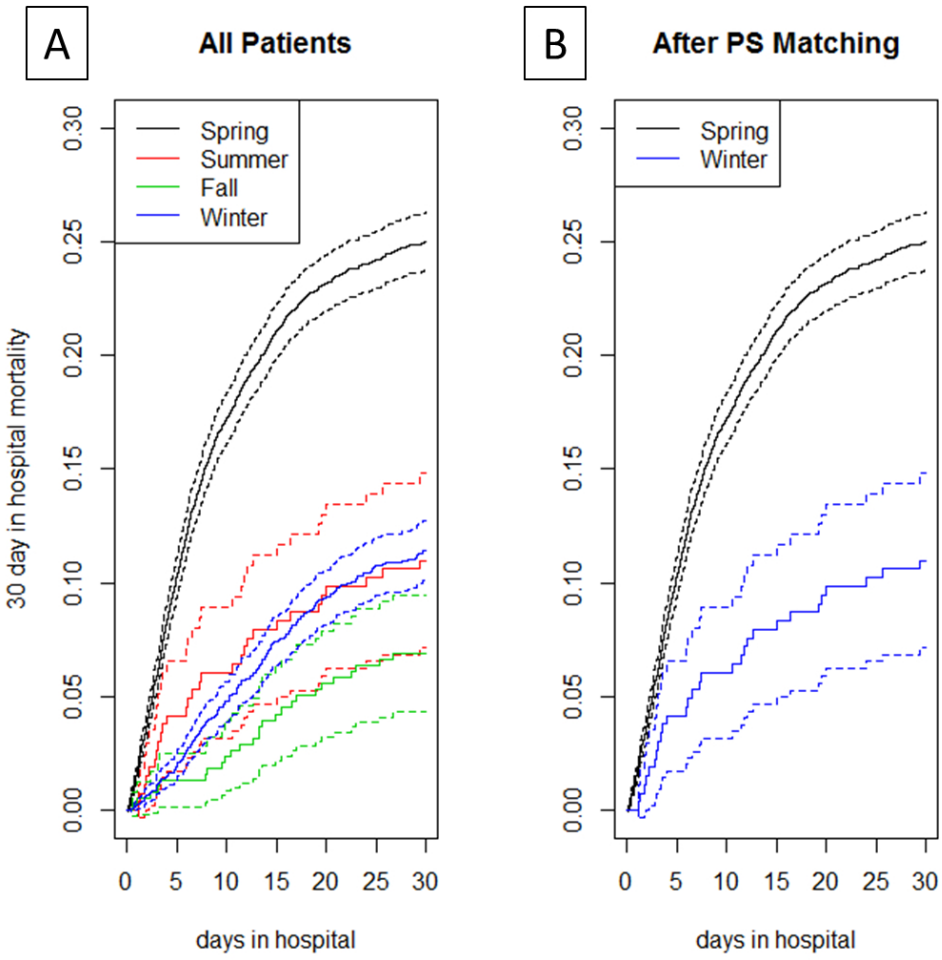

Figure 4

88x88mm (300 x 300 DPI)

Supplemental Appendix

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Supplemental Table 1 - Comparison Survivors versus Non-survivors

	Survivors (n=5953)		Non-survivors (n=1437)		p-value
	Sample	**Value**	**Sample**	**Value**	
Demographics					
Age (IQR) - yr	5953	64 (52 - 75)	1437	73 (65 - 82)	<0.001
Male sex - no (%)	5953	2989 (50.2)	1437	846 (58.9)	<0.001
Black race and / or Hispanic ethnicity – no (%)	5953	4472 (75.1)	1437	1013 (70.5)	<0.001
Body Mass Index (IQR) - kg/m^2	5679	28.4 (24.6 - 33.2)	1352	27.9 (23.8 - 32.6)	<0.001
Hospital bed saturation (IQR) - %	5953	94.1 (86.5 - 104.8)	1437	99.3 (87.5 - 107.6)	<0.001
Past Medical History					
Hypertension - no (%)	5953	4365 (73.3)	1437	1169 (81.4)	<0.001
Sleep apnea - no (%)	5953	688 (11.6)	1437	178 (12.4)	0.38
Hyperlipidemia - no (%)	5953	3366 (56.5)	1437	975 (67.8)	<0.001
Atrial fibrillation - no (%)	5953	557 (9.4)	1437	224 (15.6)	<0.001
Chronic kidney disease - no (%)	5953	1559 (26.2)	1437	622 (43.3)	<0.001
Heart failure - no (%)	5953	1181 (19.8)	1437	456 (31.7)	<0.001
Coronary artery disease - no (%)	5953	1653 (27.8)	1437	587 (40.8)	<0.001
Asthma/COPD - no (%)	5953	1842 (30.9)	1437	464 (32.3)	0.32
Diabetes mellitus - no (%)	5953	3168 (53.2)	1437	933 (64.9)	<0.001
Vitals at Presentation					
Temperature (IQR) - F	5926	99 (98 - 100)	1427	99 (98 - 100)	0.35
SBP (IQR) - mmHg	5932	132 (117 - 148)	1430	127 (107 - 146)	<0.001
DBP (IQR) - mmHg	5926	76 (67 - 85)	1428	71 (60 - 81)	<0.001
HR (IQR) – bpm	5927	96 (83 - 110)	1429	100 (85 - 114)	<0.001

Oxygen saturation (IQR) - %	5922	96 (93 - 98)	1430	92 (84 - 96)	<0.001
Respiratory Rate (IQR) - bpm	5928	19 (18 - 21)	1428	22 (19 - 26)	<0.001
Laboratory Markers					
Hemoglobin (IQR) - g/dL	5823	12.9 (11.4 - 14.1)	1408	12.6 (10.9 - 14.2)	0.006
Platelet count (IQR) -k/µL	5825	198 (137 - 264)	1408	172 (88 - 246)	<0.001
White blood cell count (IQR) - k/µL	5823	6.9 (5.1 - 9.5)	1408	8.3 (6.0 - 11.9)	<0.001
Absolute lymphocyte count (IQR) - k/µL	5880	1.1 (0.7 - 1.5)	1423	0.9 (0.6 - 1.2)	<0.001
Sodium (IQR) – mEq/L	5879	137 (134 - 140)	1428	138 (134 - 143)	<0.001
Potassium (IQR) – mEq/L	5845	4.2 (3.8 - 4.6)	1426	4.4 (4.0 – 5.0)	<0.001
Chloride (IQR) – mEq/L	5864	100 (96 - 103)	1423	100 (95 - 104)	0.28
Bicarbonates (IQR) – mEq/L	5879	24 (21 - 27)	1428	22 (18 - 25)	<0.001
Creatinine (IQR) - mg/dL	5876	1.0 (0.8 - 1.5)	1427	1.6 (1 - 2.9)	<0.001
Glucose (IQR) - mg/dL	5879	126 (104 - 179)	1428	156 (121 - 236)	<0.001
Aspartate aminotransferase (IQR) - U/L	5416	35 (24 - 55)	1312	52 (33 - 81)	<0.001
Alanine aminotransferase (IQR) - U/L	5614	26 (16 - 42)	1376	28 (18 - 46)	<0.001
Lactic acid (IQR) – mmol/L	5097	1.9 (1.4 - 2.6)	1347	2.6 (1.8 - 3.9)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	4017	384±219	926	518 (371 - 706)	<0.001
Creatine Kinase (IQR) – U/L	4714	336 (253 - 454)	1218	777±2657	<0.001
D-dimer (IQR) - µg/mL	3850	1.2 (0.7 - 2.5)	763	2.5 (1.3 - 6.9)	<0.001
Procalcitonin (IQR) – ng/mL	2800	0.1 (0.1 - 0.3)	615	0.6 (0.2 - 2.4)	<0.001
Troponin T* (IQR) - ng/mL	2365	0.01 (0.01 - 0.03)	302	0.03 (0.01 - 0.1)	<0.001
Troponin I* (IQR) – ng/mL	2684	0.01 (0.01 – 0.02)	981	0.02 (0.01 - 0.08)	<0.001
Interleukin-6 (IQR) – pg/mL	1752	17 (6 - 40)	287	68 (26- 154)	<0.001
Fibrinogen (IQR) – mg/dL	2478	570 (448 - 690)	460	621 (506 - 761)	<0.001

Ferritin (IQR) – ng/mL	3395	521 (224 - 1112)	659	1021 (514 - 2161)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Supplemental Methods

Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for in-hospital Death between Patients Spring and Winter Patients

The covariates in the multivariable analyses included factors present in > 90% of our dataset, are known to be associated with in-hospital COVID-19 mortality based on prior literature or with a univariate association between admission season (exposure) or in-hospital mortality (outcome) ($p<0.05$) and a clinical (relative difference >5%) difference between the spring and winter patients (**Supplemental Table 2**). These variables included: age, sex, BMI, vital signs at presentation, white cell count, creatinine, glucose, alanine transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Also in this model, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

Supplemental Table 2 - Comparison Spring Vs Winter

	Spring (n=4495)		Winter (n=2254)		p-value
	Sample	**Value**	**Sample**	**Value**	
Demographics					
Age (IQR) - yr	4495	66 (55 - 77)	2254	67 (56 - 77)	0.051
Male sex - no (%)	4495	2377 (52.9)	2254	1122 (49.8)	0.016
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	2254	1635 (72.5)	0.098
Body Mass Index (IQR) - kg/m^2	4229	28.4 (24.6 - 33)	2194	28.2 (24.4 - 33.1)	0.433
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6	2254	95.3 (91.9 – 101.8)	<0.001
Past Medical History					
Hypertension - no (%)	4495	3370 (75)	2254	1713 (76)	0.357
Sleep apnea - no (%)	4495	521 (11.6)	2254	270 (12)	0.640
Hyperlipidemia - no (%)	4495	2609 (58)	2254	1380 (61.2)	0.012
Atrial fibrillation - no (%)	4495	449 (10)	2254	267 (11.8)	0.019
Chronic kidney disease - no (%)	4495	1406 (31.3)	2254	620 (27.5)	0.001
Heart failure - no (%)	4495	980 (21.8)	2254	519 (23)	0.254
Coronary artery disease - no (%)	4495	1316 (29.3)	2254	721 (32)	0.022
Asthma/COPD - no (%)	4495	1371 (30.5)	2254	753 (33.4)	0.015
Diabetes mellitus - no (%)	4495	2522 (56.1)	2254	1244 (55.2)	0.475
Vitals at Presentation					
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	2254	98.7 (98.1 - 99.8)	<0.001
SBP (IQR) - mmHg	4469	131 (114 - 148)	2254	132 (117 - 148)	0.002
DBP (IQR) - mmHg	4465	75 (65 - 84)	2252	75 (67 - 84)	0.117
HR (IQR) – bpm	4467	98 (85 - 112)	2253	95 (82 - 107)	<0.001

Oxygen saturation (IQR) - %	4463	95 (91 - 98)	2253	96 (92 - 98)	<0.001
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	2254	19 (18 - 22)	<0.001
Laboratory Markers					
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	2228	12.9 (11.5 - 14.2)	0.030
Platelet count (IQR) -k/µL	4372	188 (116 - 260)	2228	196 (143 - 259)	<0.001
White blood cell count (IQR) - k/µL	4372	7.5 (5.6 - 10.6)	2228	6.4 (4.7 - 8.8)	<0.001
Absolute lymphocyte count (IQR) - k/µL	4420	1 (0.7 - 1.4)	2246	1 (0.7 - 1.4)	0.062
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	2253	137 (134 - 140)	<0.001
Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	2243	4.1 (3.8 - 4.5)	<0.001
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	2253	101 (98 - 104)	<0.001
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	2253	24 (21 - 27)	<0.001
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	2253	1.1 (0.8 - 1.5)	<0.001
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	2253	126 (104 - 184)	<0.001
Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	2084	35 (24 - 55)	<0.001
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	2171	26 (17 - 44)	0.292
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	1913	1.9 (1.4 - 2.5)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	1563	341 (254 - 468)	<0.001
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	1957	126 (67 - 282)	<0.001
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	1907	1.2 (0.7 - 2.3)	<0.001
Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	1252	0.1 (0.1 - 0.3)	<0.001
Troponin T* (IQR) - ng/mL	0	NA	2106	0.01 (0.01 - 0.03)	NA
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	0	NA	NA
Interleukin-6 (IQR) – pg/mL	1056	34 (14 - 75)	710	11 (4 - 26)	<0.001
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	1040	536 (434 - 652)	<0.001

Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	1637	510 (230 - 1094)	<0.001

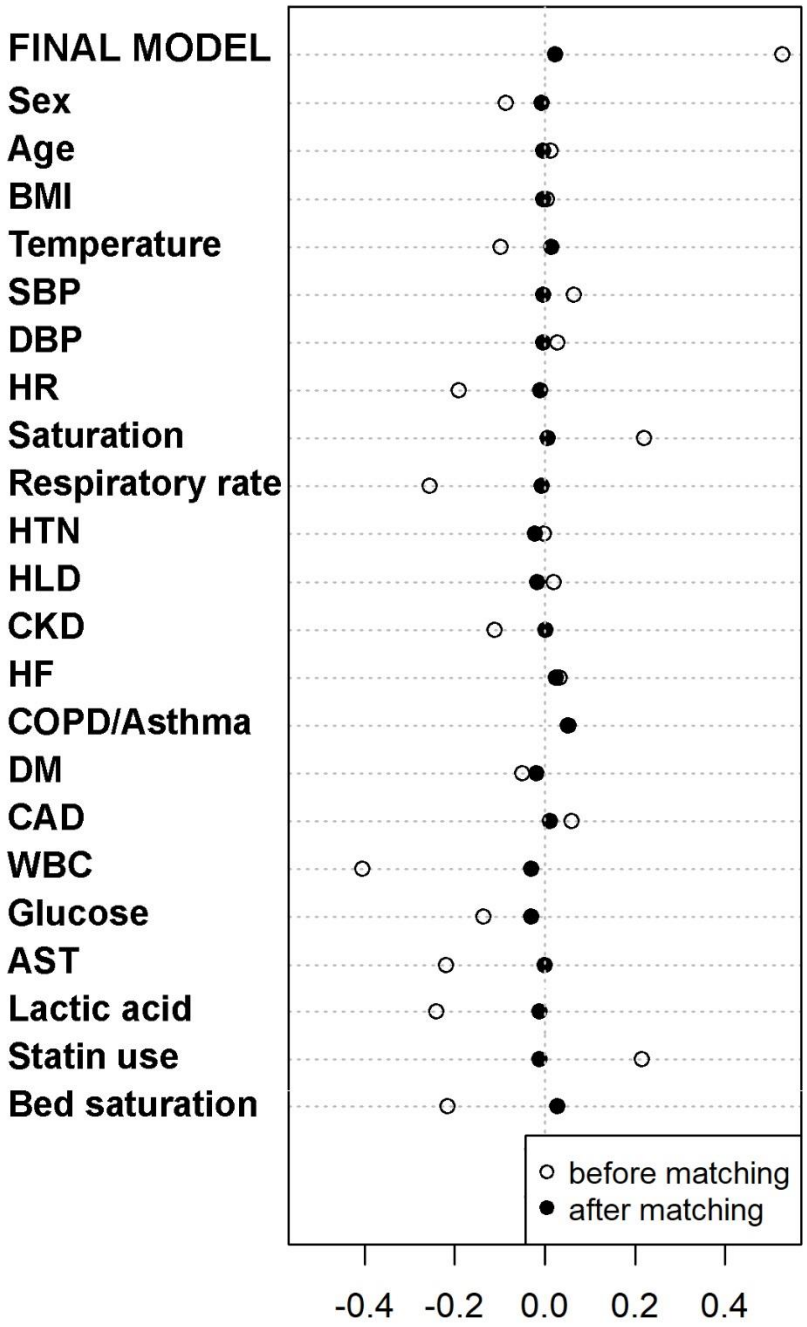
COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Supplemental Table 3 - Therapies Administered during the Admission

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
Hydroxychloroquine - no (%)	3007 (66.9)	1 (0.4)	2 (0.5)	8 (0.4)
Azithromycin - no (%)	1322 (29.4)	51 (19.3)	118 (31.3)	374 (16.6)
Other antibiotics - no (%)	3382 (75.2)	160 (60.6)	214 (56.8)	1082 (48)
Steroids - no (%)	1485 (33)	71 (26.9)	195 (51.7)	1462 (64.9)
Angiotensin-converting-enzyme Inhibitors - no (%)	318 (7.1)	36 (13.6)	51 (13.5)	269 (11.9)
Angiotensin II receptor blockers - no (%)	264 (5.9)	23 (8.7)	32 (8.5)	212 (9.4)
Statin - no (%)	1478 (32.9)	109 (41.3)	129 (34.2)	1002 (44.5)
Therapeutic anticoagulation - no (%)	1041/4496 (31.2)	76 (28.8)	98 (26.0)	772 (34.3)
Remdesivir* - no (%)	78 (1.7)	37 (14)	134 (35.5)	1224 (54.3)
Lopinavir/Ritonavir – no (%)	40 (0.9)	0 (0)	0 (0)	0 (0)
Ivermectin – no (%)	11 (0.2)	1 (0.4)	0 (0)	34 (1.5)

* 45 patients listed as remdesivir recipients in the spring season were part of a 1:1 double-blind, placebo-controlled study. Instead, all the patients in summer, fall, and winter seasons listed as remdesivir recipients received the actual medication.

Supplemental Figure 1 - Distribution of Propensity Score



AST = aspartate transaminase; BMI= body mass index; CAD= coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; DBP= diastolic blood pressure; DM = Diabetes mellitus; HF= heart failure; HLD = hyperlipidemia; HNT = hypertension; HR = heart rate; SBP = systolic blood pressure; WBC = white blood cell count

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4-5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 Supp
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12-13
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	Supp
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Hospital Bed Occupancy Rate is An Independent Risk Factor for COVID-19 Inpatient Mortality: A Pandemic Epicenter Cohort Study

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Hospital Bed Occupancy Rate is An Independent Risk Factor for COVID-19 Inpatient Mortality: A Pandemic Epicenter Cohort Study

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Abstract

Introduction: COVID-19 first struck New York City in the spring of 2020 resulting in an unprecedented strain on our health care system triggering multiple changes in public health policy governing hospital operations as well as therapeutic approaches to COVID-19. We examined inpatient mortality at our center throughout the course of the pandemic.

Methods: Retrospective chart review of clinical characteristics, treatments, and outcome data of all patients admitted with COVID-19 from March 1st, 2020 to February 28th, 2021. Patients were grouped into three-month quartiles. Hospital strain was assessed as percent of occupied beds based on a normal bed capacity of 1,491.

Results: Inpatient mortality decreased from 25.0% in spring to 10.8% over the course of the year. During this time, the use of Remdesivir, steroids, and anticoagulants increased; the use of hydroxychloroquine and other antibiotics decreased. Daily bed occupancy ranged from 62% to 118% occupancy. In a multivariate model with all year's data controlling for demographics, comorbidities, and acuity of illness, percentage of bed occupancy was associated with increased 30-day in-hospital mortality of COVID-19 patients (0.7% mortality increase for each 1% increase in bed occupancy - HR 1.007, CI: 1.001, 1.013, p=0.004)

Conclusion: Inpatient mortality from COVID-19 was associated with bed occupancy. Early reduction in epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

Strengths and limitations of this study

- Large cohort study (7,390 COVID-19 patients).
- Longitudinal analysis over 1 year of management and hospital policy changes.
- Analysis of mortality changes after adjustment for different therapies and clinical parameters.
- Identification of the association between level of hospital system stress and mortality, with important public health ramifications.
- Limitation: data on most recent variants are not included

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization on March 11th, 2020.[1] In the United States, after a cluster of cases reported from Washington state[2], New York state quickly became the initial epicenter of this pandemic with over 1.27 million of cases till date and over 50,000 fatalities with the highest concentration in the Bronx and Queens boroughs of New York City .[3] Montefiore Einstein, with its three principal teaching hospitals and combined adult bed capacity of 1,491, is the primary health care provider for the large, nearly 1.5 million diverse population of the Bronx[4] and experienced a "first wave" of COVID-19 admissions in the spring of 2020 [3], followed by a significant reduction of cases until a second surge in hospitalizations was noted in the winter of 2020. Throughout the course of the year, multiple public health measures - including those adapting hospital operation to a disaster level pandemic, such as cancellation of all elective procedures and waiver of state specific licensing for health care providers - were put in place. In addition, the understanding of COVID-19 pathophysiology improved [5 6], new treatments were developed [7-10], parts of the general population[11 12] as well as hospital personnel developed antibodies after COVID-19 illness [13], and our hospital system adapted to and then recovered from crisis mode.[14] Here, we report outcomes of patients hospitalized with COVID-19 through one year since the first case, focusing on the differences observed between the spring and the winter surges.

METHODS:

Study Population

We retrospectively reviewed all adult patients admitted to Montefiore Medical Center with a real time reverse transcription polymerase chain reaction (RT-PCR) assay positive for COVID-19

between March 1, 2020 and February 28, 2021. We divided this timeframe in four 3-month seasons based on northern hemisphere calendar: spring (March 1, 2020 to May 31, 2020), summer (June 1, 2020 to August 30, 2020), fall (September 1, 2020 to November 30, 2020), and winter (December 1, 2020 to February 28, 2021).

Data Collection

Medical data including demographic, clinical, and laboratory variables were extracted from the electronic medical record system. The primary outcome was 30-day in-hospital mortality.

Statistical Analysis

Continuous variables are displayed as mean ± standard deviation or median [25-75% interquartile range] and compared with the Student's t-test, or Wilcoxon ranks-sum, as appropriate. Categorical data are presented as percent and compared by the chi-squared test. We estimated the cumulative incidence of the primary endpoint in-hospital mortality for each season, treating hospital discharge as a competing event.[15] To avoid any bias due to differential follow-up length, we censored the follow-up time at 30 days after the admission.

A multivariable competing risk proportional hazard models was used to estimate the sub-distribution hazard ratios[16 17] for time to in-hospital death. The covariates in the multivariable analyses included factors present in > 90% of our dataset, known to be associated with in-hospital COVID-19 mortality based on prior literature[6 18 19], or with a univariate association with in-hospital mortality ($p<0.05$) and a clinical (relative difference >5%) difference between survivors and non survivors (**Supplemental Table 1**). These variables included: age, sex, body mass index (BMI), vital signs at presentation (temperature, systolic and diastolic blood pressure,

heart rate, respiratory rate, pulse oxygen saturation), platelet count, white cell count, potassium, bicarbonate, creatinine, glucose, alanine transaminase, aspartate transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Additionally, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

Then we focused on examining the difference in in-hospital death between patients admitted in the spring and in the winter, as they represented the two largest and most temporal distant waves of the COVID-19 pandemic occurring before and after public health polices, specific therapeutic approaches and hospital management changes had been implemented. Selection method for covariates is presented in the **Supplemental Material** and **Supplemental Table 2**.

The proportionality assumption was examined [20] and no violation was identified. A two-sided $p<0.05$ was considered statistically significant.

Propensity Score Analysis

To fully control the potential differences in patient population and hospital stress between spring and winter COVID-19 patients, we also used propensity score (PS) matching to compare the 30-day in-hospital mortality between spring and winter admissions. The same covariates used for the multivariable competing risk regression were used for PS matching. PS matching was carried out through a 1:1 greedy matching algorithm, with a caliper width of 0.1 SD. We then stratified on matched pair in the competing risk regression model.[21 22] Because one-to-one matching led to a reduction in sample size, we used this analysis as a sensitivity analysis.

All statistical analyses was performed with SPSS (IBM Corp, ver. 25, Armonk, NY) and the R packages cmprsk and crrSC (R Foundation for Statistical Computing, ver 3.5)

Patient and Public Involvement

Given the retrospective nature of our analysis, it was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

7,390 COVID-19 positive adult patients were admitted between March 1, 2020 and February 28, 2021 (**Figure 1**). 4,495 patients were admitted during the spring, 264 during the summer, 377 during the fall, and 2,254 during the winter.

On April 8, 2020, peak of the spring season, the total numbers of simultaneously adult patients admitted to our hospital (including those admitted to emergency adult wards at our children's hospital[23]) was 1,762 (118% of nominal bed capacity); 1,201 of them (68.2%) were COVID-19 patients. On February 8, 2021, peak of winter season, 1,512 patients (101% of nominal bed capacity) were admitted to our hospital and 393 of them (26.0%) were COVID-19 patients. (**Figure 1**). Following cancellation of elective procedures, bed occupancy decreased to 70% by the end of the spring season and remained at 90% until the beginning of the winter season, when the second wave occurred in December 2020. Unadjusted mortality for patient admitted at the beginning of spring, end of spring, beginning of winter, and end of winter was 28%, 8%, 14%, and 13%, respectively (**Figure 2**).

Patient Population

Demographics, past medical history, vital signs at arrivals are presented in **Table 1**. Initial laboratory blood tests are presented in **Supplemental Table 3.** Overall, median age was 66 (55 – 77) years, 3,835 (51.9%) patients were male, 5,519 (74.2%) were of Black race and/or Hispanic ethnicity. Median age ranged from 63 years (fall) to 67 years (spring). Sex distribution was similar throughout the year. Summer and fall patients had the lowest and the highest BMI: 26.7 and 28.6 kg/m^2, respectively.

Pharmacotherapy

Changes in pharmacological approach is presented in **Supplemental Table 4** and **Figure 3.** Spring patients were more likely to receive hydroxychloroquine, azithromycin and other antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2% during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of statins, angiotensin converting inhibitors (ACE-I), or angiotensin receptor blockers (ARBs) also increased.

Death, Intubation, and Length of Stay

Over the course of a year, 1,437 (19.4%) died while hospitalized. Patients who died were older, had more comorbidities, and were more acutely ill consistent within prior reports on risk factors for death in COVID-19[5 6] (**Supplemental Table 1**). Average unadjusted monthly mortality is presented in **Figure 2**. 30-day in-hospital mortality (**Figure 4A**) was 25.0% for the spring patients, 11.0% for summer patients, 6.9% for fall patients, and 11.4% for winter patients

(p<0.001). On average, spring patients died 6.4 (3.2 – 12.9) days after the arrival to the emergency department, summer patients 7.2 (3.0 – 15.7) days after the arrival, fall patients 13.4 (8.7 – 21.6) days after arrival, and winter patients 13.3 (6.8 – 20.7) days after the arrival (p<0.001). Frequency of invasive ventilatory support was higher during the spring with 892 patients (19.4%) intubated, versus 27 (10.2%) in the summer, 36 (9.5%) during fall, and 268 (11.9%) in the winter, p<0.001. Median time from arrival-to-intubation was 0.7 (0.1 - 4.1) days for spring patients, 0.6 (0.1 - 8.1) days for summer patients, 2.2 (0.1 – 7.3) days for fall patients, and 2.8 (0.3 – 7.0) days for winter patients, p<0.001. Median length of stay was 6.1 (3.5 – 11.1) days during spring, 5.1 (2.7 – 10.1) days during summer, 5.0 (3.0 – 10.1) days during fall, and 6.3 (3.8 – 12.0) days during winter, p<0.001.

Bed Saturation and Mortality

We defined bed saturation the percentage of bed occupancy calculated from the ratio between the number of admitted patients over the nominal bed capacity of our institution (1,491).

In the multivariable competing risk proportional hazard model of the entire cohort, percent of bed occupancy was associated with increased 30-day in-hospital mortality (HR 1.007, CI: 1.001, 1.013, p=0.004); i.e mortality increase by 0.7 % for each 1% increase of bed occupancy. Consistent results were observed per level increase in bed occupancy quartile, (HR 1.086 [1.026 -1.148], P-value for linear trend = 0.004). Results of the competing risk regression analysis are presented in the **Table 2.**

Spring vs Winter Mortality Comparison and Propensity Matched Analysis

In the multivariable competing risk proportional hazard model comparing spring and winter season, 30-day in-hospital mortality was lower in winter (HR 0.520, CI 0.448-0.604, p<0.001) when compared to spring. After PS caliper matching, there were 1,722 matched pairs. Spring and winter patients had similar distribution of PS (**Supplemental Figure 1**) and standardized average difference among covariates was greatly reduced. PS analysis showed a significant reduction of in-hospital mortality during winter (HR 0.580 CI: 0.507-0.663, p<0.001) confirming what we observed in the multivariable adjusted analysis (**Figure 4B**).

DISCUSSION

We examined inpatient mortality from COVID-19 over the course of a one-year pandemic at our hospital system in New York City. Our principal findings are as follows: First, we observed a substantial reduction of in-hospital mortality coinciding with multiple pandemic related public health measures focusing on hospital resource management – and preceding comprehensive changes in pharmacotherapy - towards the end of the first surge. Second, we describe - for the first time - hospital bed occupancy as an independent risk factor for inpatient mortality from COVID-19.

Public Health Measures in Response to COVID-19

After declaring a state of disaster emergency (March 7, 2020), New York State introduced different measures to limit the spread of the disease, including public schools closure (March 16, 2020), limitation of indoor dining (March 17, 2020), stay-home order for non-essential workers (March 22, 2020), mandatory face coverings in public (April 15, 2020), and night subway closure (April 30, 2020)[24]. Despite these measures to limit the diffusion of the disease and a

generalized reduction of movements around New York City (as evidenced by a more than 90% reduction of subway ridership compared to 2019)[25], more than 30% of Bronx residents were found to have positive antibodies (and thus possibly temporary immunity) against SARS-CoV-2 in August 2020.[26]

Specifically relevant to hospital operations, executive order no. 202.5 (March 16, 2020)[27] allowed healthcare providers not licensed or registered in New York State to temporarily work in the State, and executive order no. 202.10 (March 22, 2020)[27] suspended elective operations. These executive orders were associated with a dramatic drop in non-COVID-19 admissions at our institution beginning March 16, 2020. (**Figure 1**). On March 26, 2020 New York State Governor Cuomo additionally mandated all hospitals to increase their bed capacity by 50% to accommodate the surge of COVID-19 patients.[27] Despite this order, the actual bed occupancy at our institution (while accommodating all COVID-19 patients presenting to our hospitals) remained below the usual operating capacity until December 2020.

Notably, COVID-19 mortality remained stable throughout the summer and fall 2020 with low case counts and increased utilization of steroids, anticoagulation, and remdesivir. Although randomized controlled trials have shown morbidity benefits with the use of remdesevir[7] and mortality reduction with steroids[8], the magnitude of these effects cannot explain the more than 50% reduction in mortality we observed. Furthermore, pharmacotherapy, with the exception of hydroxychloroquine elimination, did not materially change within the spring season, by the end of which mortality was already decreased. Steroid, remdesivir, and therapeutic anticoagulation were used in 10-20% of patients by May 2020, but they reached 30-70% only in the winter season. Despite that, unadjusted mortality began to increase again in December 2020 during the

second wave. Of note, bed occupancy also increased at that time and proved to be an independent risk factor for COVID-19 mortality in our cohort of nearly 8,000 patients.

Change in Therapeutic Approach

The initial widespread (>2/3 of first spring patients) use of hydroxychloroquine, an agent eventually proven to be ineffective[28] to treat COVID-19, probably represents the most obvious pandemic-associated deviation from the usual multiphase clinical trial standards of therapeutic paradigm development. Only 8 of 2,254 patients received hydroxychloroquine during the winter wave. Similarly, we observed a reduction in the use of azithromycin and other antibiotics, the latter possibly reflecting a more careful assessment of the need to treat superimposed bacterial infections during the second wave. Steroid therapy[8 29] and therapeutic anticoagulation[9] were implemented in the majority of patients during the winter after the knowledge on the likely disease modulating inflammatory proprieties and pro-thrombotic effect of COVID-19 had been recognized[30] and, in the case of steroids, a therapeutic effect had been proven[8]. Remdesivir, an inhibitor of the viral RNA-dependent RNA polymerase that showed shortening of recovery time in hospitalized patients with COVID-19 [7], received emergency FDA approval on October 22nd,2020 [31] and was administered to almost half of the admitted patients during the winter. If initial concerns of possible interactions between ACE-I or ARBs and SARS-CoV-2 [32] led to a possible underutilization or discontinuation of these drugs during the spring, we observed a significant increase in their use during the following months, after no increased risks were reported. [33 34]

Similarly, after several reports showed a possible protective effect associated with the use of statins[35 36], their utilization markedly increased during the winter.

Lastly, after the spring wave provided anecdotal evidence for early proning in COVID-19 pneumonia, an approach strongly favoring noninvasive ventilation and avoiding intubation was developed to address respiratory distress in COVID-19; more data about such an approach has since accumulated. [10 37] The cumulative effect of these therapeutic changes, in combination with a better preparedness to respond to a pandemic, can be estimate from the different mortality between the first surge (spring) and the second surge (winter). After matching the two groups for demographic and clinical variables, as well as for elements indicative of hospital distress (bed occupancy), a significant reduction of mortality was observed during the winter trimester.

Change in Hospital Stress Load

At the peak of the pandemic, the hospital saturation reached the 118% of the nominal bed capacity and COVID-19 patients accounted for 68.2% of all admitted patients. This increase in acutely ill patients created significant excess demand on the rest of the hospital infrastructure best characterized by the surge in the need for intensive care unit (ICU) beds and transformation of other hospital areas to ICUs.[14 23] Despite increased patient load, the number of standard ICU beds, as well as laboratories, diagnostic equipment, and available personnel, remained the same as before the pandemic. This unmatched patient overload resulted in a 0.7 % mortality increase for each 1% increment in hospital bed saturation. In light of these results, strategies to minimize the bed occupancy for non-Covid-19 patients or non-life-saving admission should be adopted to diverge resources to improve the outcome of admitted Covid-19 patients.

Limitations

Our study has the shortcomings of a retrospective investigation, but there are some very specific aspects limiting the interpretation of our results. First, it is difficult to assess the true effects of pharmacotherapy given the dynamic changes in indications, doses, and usage that happened over the course of the year. Regardless, we believe the propensity-matched comparison between the spring and the winter waves provides compelling evidence for the validity of our principal observation of inpatient COVID-19 mortality reduction disproportionate to advances in pharmacotherapy. We chose total bed occupancy as a metric for hospital stress assuming that other resources per bed remained static. Notably, the ratio of COVID-19 to non-COVID-19 patients, ICU bed saturation, and staff shortages are unaccounted for in this model. Regrettably, an in-depth analysis of these metrics is beyond our ability in this retrospective pandemic analysis with disaster elements. Additionally, a significant number of patients received ICU-level-of-care interventions (mechanical ventilatory support, dialysis, vasopressors titration) on regular floors; therefore, the concept of ICU bed saturation might have been not truly representative of the burden.

However, we feel our data is sufficiently strong to support the notion that bed capacity expansion alone is not the answer. Rather, a smaller number of beds with higher staffing accomplished by drastic reductions in all non-emergent procedures and activities is likely a better approach. Although offering fewer beds in pandemic situation appears initially quite counterintuitive, in practice we observed that mortality began to decrease once beds and resources were allocated specifically to COVID-19 patients by executive orders 202.5 and 202.10; and most importantly that bed occupancy never exceeded 100% once hospital operations focused on the COVID-19 pandemic only. It is conceivable that an uptrend in mortality observed late in the pandemic with established treatment paradigms could be due to new viral strains or a sicker patient population.

Although we are unable to provide detailed strain analysis for our study population, a meaningful numbers of new (and possibly more virulent) strains were not yet observed in in the Bronx, where our study was conducted.[38] The small sample size of patients in summer and fall does not allow meaningful propensity matched comparisons, and when comparing summer, fall, and winter populations, there do not appear to be clinically meaningful differences. Lastly, single-patient data on vaccination status were not available. At the conclusion of the study, only 13.8% of the population of New York State received at least one dose and 7.4% received two doses[39]. Given the heterogeneous distribution of vaccination within the state (and the city of New York), it is impossible to meaningfully account for these parameters.

CONCLUSIONS

Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in disease specific therapeutics. Increased bed occupancy was associated to a higher in-hospital mortality. Implementation of non-pharmacological approaches and other seasonal variations might also had a role in the mortality reduction.. Early reduction in epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

DECLARATIONS

Ethics approval and consent to participate

The Office of Human Research Affairs at Albert Einstein College of Medicine approved this study (# 2020-11308). Patient consent and HIPAA forms were waived by our IRB due to the retrospective nature of our research.

Consent for publication

Non applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

No conflicts of interest exist.

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Author's Contributions

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Underlying data verified by FC, XX, and UPJ.

Acquisition, analysis, and interpretation of data: FC, XX, OS, RK, YAP, SRP, MJG, ADR, DS, and UPJ.

Statistical analysis: FC and XX.

Obtained funding: UPJ

Manuscript writing: FC, XX, and UPJ.

Critical revision of the manuscript for important intellectual content: FC, XX, OS, RK, YAP, SRP, MJG, ADR, DS, and UPJ.

Supervision: UPJ

All the Authors reviewed the work and approved the final version.

FC and UPJ had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Demographics, Past Medical History, and Vital Signs of Admitted Patients

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
30-Day hospital outcome				
Still admitted - no (%)	194 (4.3)	6 (2.3)	15 (4.0)	103 (4.6)
Discharged alive - no (%)	3177 (70.7)	229 (86.7)	336 (89.1)	1893 (84.0)
Dead in the hospital - no (%)	1124 (25.0)	29 (11.0)	26 (6.9)	258 (11.4)
Demographics				
Age (IQR) – yr	66 (55 - 77)	66 (50 - 76)	63 (50 - 73)	67 (56 - 77)
Male sex - no (%)	2377 (52.9)	138 (52.3)	198 (52.5)	1122 (49.8)
Black race and / or Hispanic ethnicity – no (%)	3345 (74.4)	219 (83.0)	286 (75.9)	1635 (74.2)
Body Mass Index (IQR) - kg/m^2	28.4 (24.6 - 33)	27.6 (22.5 - 32.7)	28.6 (25 - 34.1)	28.2 (24.4 - 33.1)
Hospital bed saturation (IQR) - %	97.4 (86.5 – 107.6)	81.7 (76.3 – 85.8)	87.6 (83.2 - 90.2)	95.3 (91.9 – 101.8)
Past Medical History				
Hypertension - no (%)	3370 (75)	197 (74.6)	254 (67.4)	1713 (76)
Sleep apnea - no (%)	521 (11.6)	28 (10.6)	47 (12.5)	270 (12)
Hyperlipidemia - no (%)	2609 (58)	153 (58)	199 (52.8)	1380 (61.2)
Atrial fibrillation - no (%)	449 (10)	30 (11.4)	35 (9.3)	267 (11.8)
Chronic kidney disease - no (%)	1406 (31.3)	70 (26.5)	85 (22.5)	620 (27.5)
Heart failure - no (%)	980 (21.8)	72 (27.3)	66 (17.5)	519 (23)
Coronary artery disease - no (%)	1316 (29.3)	95 (36)	108 (28.6)	721 (32)
Asthma/COPD - no (%)	1371 (30.5)	84 (31.8)	98 (26)	753 (33.4)
Diabetes mellitus - no (%)	2522 (56.1)	148 (56.1)	187 (49.6)	1244 (55.2)
Vitals at Presentation				
Temperature (IQR) - F	98.9 (98.2 - 100)	98.4 (97.8 - 98.9)	98.8 (98.1 - 99.9)	98.7 (98.1 - 99.8)
SBP (IQR) - mmHg	131 (114 - 148)	132 (117 - 149)	131 (117 - 147)	132 (117 - 148)
DBP (IQR) - mmHg	75 (65 - 84)	77 (67 - 87)	74 (68 - 84)	75 (67 - 84)
HR (IQR) – bpm	98 (85 - 112)	92.5 (76.3 - 105)	94 (80 - 107)	95 (82 - 107)
Oxygen saturation (IQR) - %	95 (91 - 98)	98 (96 - 99)	96 (94 - 98)	96 (92 - 98)
Respiratory Rate (IQR) - bpm	20 (18 - 22)	18 (17 - 20)	18 (18 - 20)	19 (18 - 22)

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure.

Table 2. Association with In-Hospital Mortality (Regression models with competing risks)

	Multivariable	
Variable	**HR (95% CI)**	**P-value**
Age - yr	1.046 (1.04 - 1.051)	<0.001
Male sex - yes/no	1.352 (1.187 - 1.54)	<0.001
Body mass index - kg/m2	1.022 (1.012 - 1.032)	<0.001
Temperature - F	1.071 (1.036 - 1.108)	<0.001
SBP - mmHg	0.994 (0.991 - 0.997)	<0.001
DBP - mmHg	0.996 (0.991 - 1.001)	0.14
HR - bpm	1.003 (0.999 - 1.006)	0.11
Oxygen saturation - %	0.967 (0.961 - 0.972)	<0.001
Respiratory rate - bpm	1.027 (1.019 - 1.035)	<0.001
White blood cell count - k/µL	1.008 (1.001 - 1.016)	0.02
Glucose - mg/dL	1.001 (1 - 1.001)	0.001
Aspartate aminotransferase - U/L	1 (1 - 1.001)	0.21
Alanine aminotransferase - U/L	1 (0.999 - 1)	0.25
Lactic acid – mmol/L	1.071 (1.036 - 1.107)	<0.001
Platelet count -k/µL	0.999 (0.998 - 0.999)	<0.001
Potassium – mEq/L	1.096 (1.028 - 1.168)	0.0052
Bicarbonates – mEq/L	0.957 (0.944 - 0.971)	<0.001
Creatinine - mg/dL	1.023 (0.998 - 1.049)	0.069
HTN - yes/no	1.008 (0.851 - 1.194)	0.93
HLD - yes/no	1.196 (1.02 - 1.401)	0.027
CKD - yes/no	1.263 (1.09 - 1.462)	0.002
HF - yes/no	1.33 (1.146 - 1.543)	<0.001
COPD/Asthma - yes/no	0.948 (0.827 - 1.088)	0.45
DM - yes/no	0.946 (0.819 - 1.093)	0.45
CAD - yes/no	1.101 (0.955 - 1.271)	0.19
Statin use - %	0.577 (0.501 - 0.664)	<0.001
Bed occupancy - %	1.007 (1.001 - 1.013)	0.004

CAD = Coronary artery disease; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; DM= Diabetes mellitus; HLD = hyperlipidemia; HF = Heart failure; HR = Heart rate; HTN = Hypertension; SBP = Systolic blood pressure

Figure Legends

Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

Figure 2. Cumulative Monthly Admissions and Mortality

Cumulative monthly admissions (black line, left axis) and mortality (dotted red line, right axis) over the year.

Figure 3. Change in Therapies

Percent of patients receiving specific therapies over the year.

Figure 4. Cumulative Incidences

30-day in-hospital mortality by seasons.

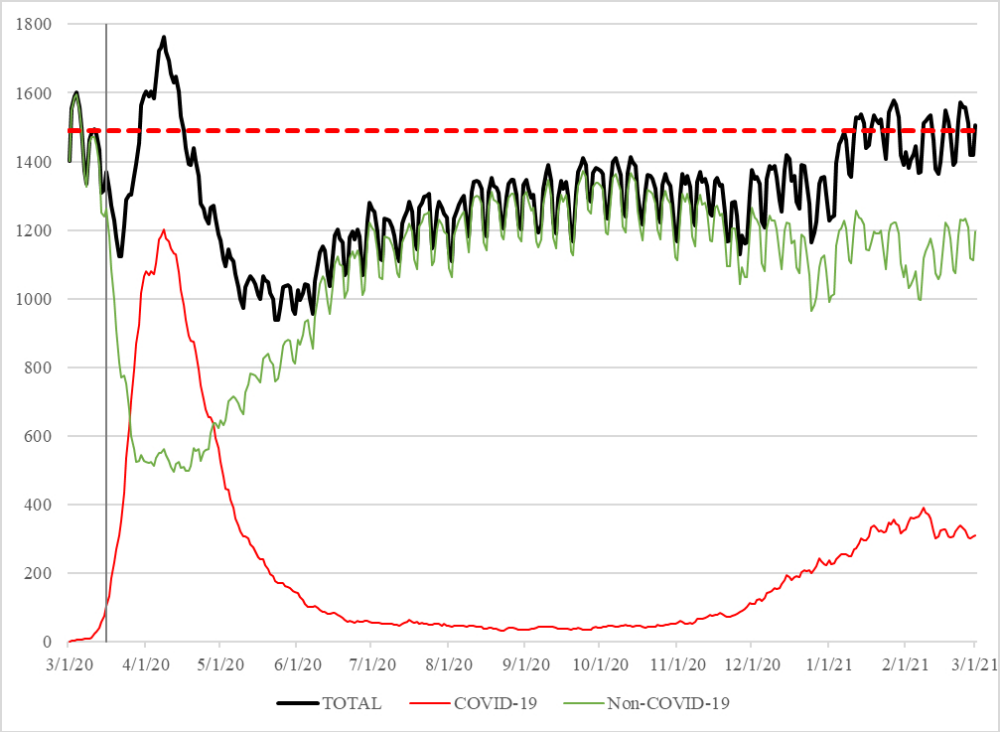

Figure 1. Simultaneously Admitted Patients
This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

85x62mm (300 x 300 DPI)

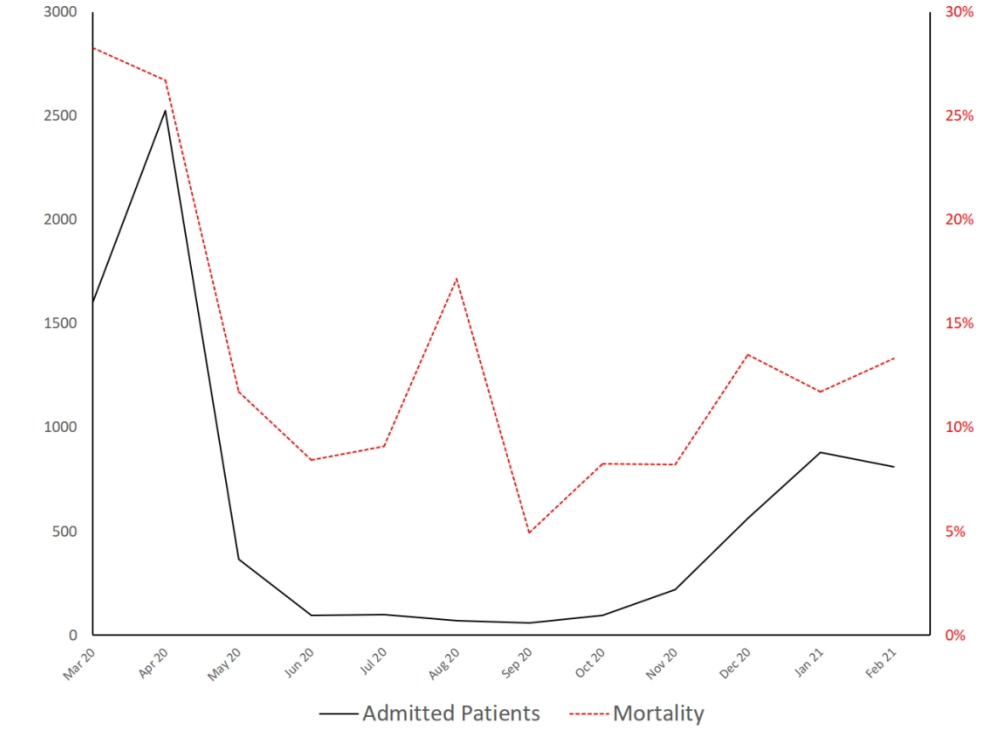

Figure 2. Cumulative Monthly Admissions and Mortality
Cumulative monthly admissions (black line, left axis) and mortality (dotted red line, right axis) over the year.

111x87mm (300 x 300 DPI)

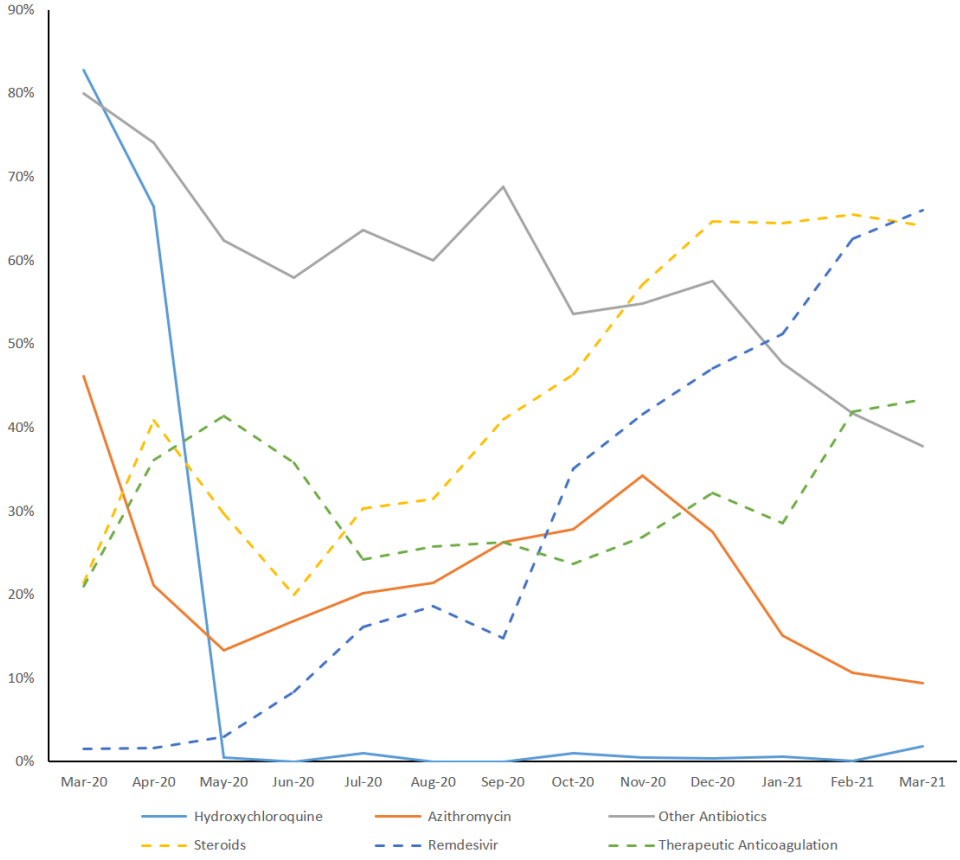

Figure 3. Change in Therapies
Percent of patients receiving specific therapies over the year.

97x85mm (300 x 300 DPI)

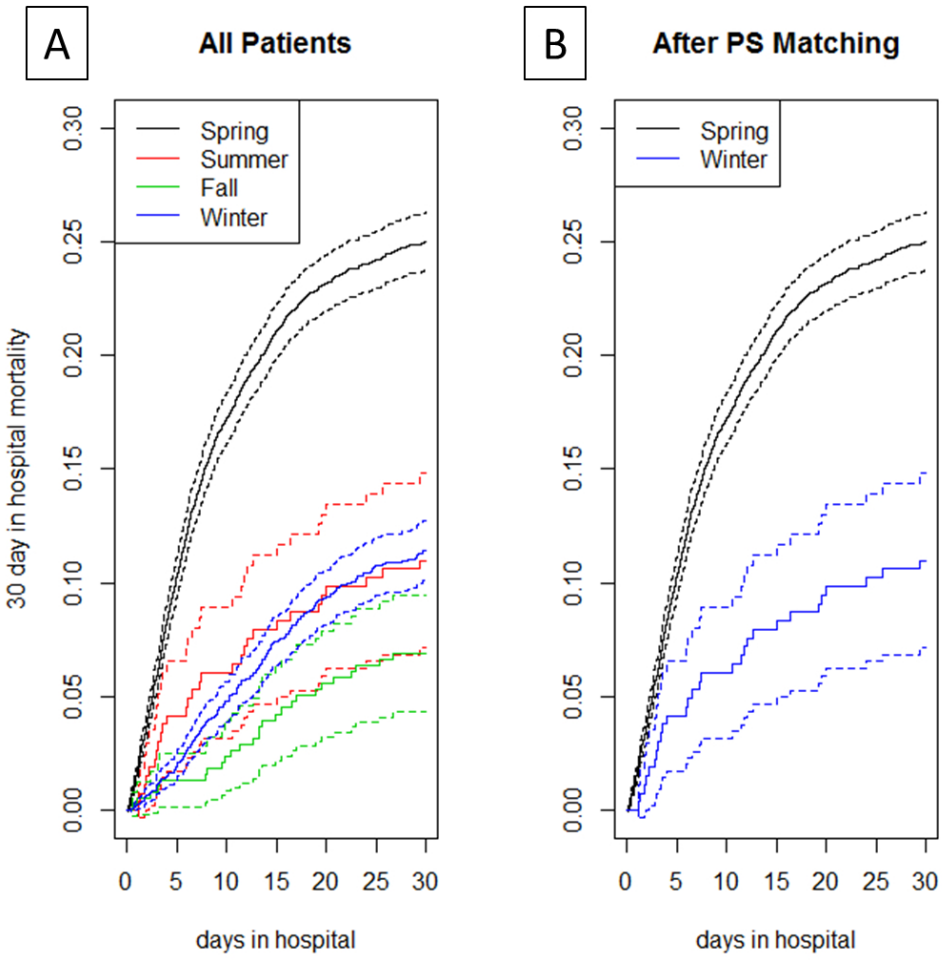

Figure 4. Cumulative Incidences

30-day in-hospital mortality by seasons.

88x88mm (300 x 300 DPI)

Supplemental Appendix

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Supplemental Table 1 - Comparison Survivors versus Non-survivors

	Survivors (n=5953)		Non-survivors (n=1437)		p-value
	Sample	**Value**	**Sample**	**Value**	
Demographics					
Age (IQR) - yr	5953	64 (52 - 75)	1437	73 (65 - 82)	<0.001
Male sex - no (%)	5953	2989 (50.2)	1437	846 (58.9)	<0.001
Black race and / or Hispanic ethnicity – no (%)	5953	4472 (75.1)	1437	1013 (70.5)	<0.001
Body Mass Index (IQR) - kg/m^2	5679	28.4 (24.6 - 33.2)	1352	27.9 (23.8 - 32.6)	<0.001
Hospital bed saturation (IQR) - %	5953	94.1 (86.5 - 104.8)	1437	99.3 (87.5 - 107.6)	<0.001
Past Medical History					
Hypertension - no (%)	5953	4365 (73.3)	1437	1169 (81.4)	<0.001
Sleep apnea - no (%)	5953	688 (11.6)	1437	178 (12.4)	0.38
Hyperlipidemia - no (%)	5953	3366 (56.5)	1437	975 (67.8)	<0.001
Atrial fibrillation - no (%)	5953	557 (9.4)	1437	224 (15.6)	<0.001
Chronic kidney disease - no (%)	5953	1559 (26.2)	1437	622 (43.3)	<0.001
Heart failure - no (%)	5953	1181 (19.8)	1437	456 (31.7)	<0.001
Coronary artery disease - no (%)	5953	1653 (27.8)	1437	587 (40.8)	<0.001
Asthma/COPD - no (%)	5953	1842 (30.9)	1437	464 (32.3)	0.32
Diabetes mellitus - no (%)	5953	3168 (53.2)	1437	933 (64.9)	<0.001
Vitals at Presentation					
Temperature (IQR) - F	5926	99 (98 - 100)	1427	99 (98 - 100)	0.35
SBP (IQR) - mmHg	5932	132 (117 - 148)	1430	127 (107 - 146)	<0.001

DBP (IQR) - mmHg	5926	76 (67 - 85)	1428	71 (60 - 81)	<0.001
HR (IQR) – bpm	5927	96 (83 - 110)	1429	100 (85 - 114)	<0.001
Oxygen saturation (IQR) - %	5922	96 (93 - 98)	1430	92 (84 - 96)	<0.001
Respiratory Rate (IQR) - bpm	5928	19 (18 - 21)	1428	22 (19 - 26)	<0.001
Laboratory Markers					
Hemoglobin (IQR) - g/dL	5823	12.9 (11.4 - 14.1)	1408	12.6 (10.9 - 14.2)	0.006
Platelet count (IQR) -k/µL	5825	198 (137 - 264)	1408	172 (88 - 246)	<0.001
White blood cell count (IQR) - k/µL	5823	6.9 (5.1 - 9.5)	1408	8.3 (6.0 - 11.9)	<0.001
Absolute lymphocyte count (IQR) - k/µL	5880	1.1 (0.7 - 1.5)	1423	0.9 (0.6 - 1.2)	<0.001
Sodium (IQR) – mEq/L	5879	137 (134 - 140)	1428	138 (134 - 143)	<0.001
Potassium (IQR) – mEq/L	5845	4.2 (3.8 - 4.6)	1426	4.4 (4.0 – 5.0)	<0.001
Chloride (IQR) – mEq/L	5864	100 (96 - 103)	1423	100 (95 - 104)	0.28
Bicarbonates (IQR) – mEq/L	5879	24 (21 - 27)	1428	22 (18 - 25)	<0.001
Creatinine (IQR) - mg/dL	5876	1.0 (0.8 - 1.5)	1427	1.6 (1 - 2.9)	<0.001
Glucose (IQR) - mg/dL	5879	126 (104 - 179)	1428	156 (121 - 236)	<0.001
Aspartate aminotransferase (IQR) - U/L	5416	35 (24 - 55)	1312	52 (33 - 81)	<0.001
Alanine aminotransferase (IQR) - U/L	5614	26 (16 - 42)	1376	28 (18 - 46)	<0.001
Lactic acid (IQR) – mmol/L	5097	1.9 (1.4 - 2.6)	1347	2.6 (1.8 - 3.9)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	4017	384±219	926	518 (371 - 706)	<0.001
Creatine Kinase (IQR) – U/L	4714	336 (253 - 454)	1218	777±2657	<0.001
D-dimer (IQR) - µg/mL	3850	1.2 (0.7 - 2.5)	763	2.5 (1.3 - 6.9)	<0.001
Procalcitonin (IQR) – ng/mL	2800	0.1 (0.1 - 0.3)	615	0.6 (0.2 - 2.4)	<0.001
Troponin T* (IQR) - ng/mL	2365	0.01 (0.01 - 0.03)	302	0.03 (0.01 - 0.1)	<0.001
Troponin I* (IQR) – ng/mL	2684	0.01 (0.01 – 0.02)	981	0.02 (0.01 - 0.08)	<0.001

Interleukin-6 (IQR) – pg/mL	1752	17 (6 - 40)	287	68 (26- 154)	<0.001
Fibrinogen (IQR) – mg/dL	2478	570 (448 - 690)	460	621 (506 - 761)	<0.001
Ferritin (IQR) – ng/mL	3395	521 (224 - 1112)	659	1021 (514 - 2161)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Supplemental Methods

Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for in-hospital Death between Patients Spring and Winter Patients

The covariates in the multivariable analyses included factors present in > 90% of our dataset, are known to be associated with in-hospital COVID-19 mortality based on prior literature or with a univariate association between admission season (exposure) or in-hospital mortality (outcome) ($p<0.05$) and a clinical (relative difference >5%) difference between the spring and winter patients (**Supplemental Table 2**). These variables included: age, sex, BMI, vital signs at presentation, white cell count, creatinine, glucose, alanine transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Also in this model, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

Supplemental Table 2 - Comparison Spring Vs Winter

	Spring (n=4495)		Winter (n=2254)		p-value
	Sample	Value	Sample	Value	
Demographics					
Age (IQR) - yr	4495	66 (55 - 77)	2254	67 (56 - 77)	0.051
Male sex - no (%)	4495	2377 (52.9)	2254	1122 (49.8)	0.016
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	2254	1635 (72.5)	0.098
Body Mass Index (IQR) - kg/m^2	4229	28.4 (24.6 - 33)	2194	28.2 (24.4 - 33.1)	0.433
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6	2254	95.3 (91.9 – 101.8)	<0.001
Past Medical History					
Hypertension - no (%)	4495	3370 (75)	2254	1713 (76)	0.357
Sleep apnea - no (%)	4495	521 (11.6)	2254	270 (12)	0.640
Hyperlipidemia - no (%)	4495	2609 (58)	2254	1380 (61.2)	0.012
Atrial fibrillation - no (%)	4495	449 (10)	2254	267 (11.8)	0.019
Chronic kidney disease - no (%)	4495	1406 (31.3)	2254	620 (27.5)	0.001
Heart failure - no (%)	4495	980 (21.8)	2254	519 (23)	0.254
Coronary artery disease - no (%)	4495	1316 (29.3)	2254	721 (32)	0.022
Asthma/COPD - no (%)	4495	1371 (30.5)	2254	753 (33.4)	0.015
Diabetes mellitus - no (%)	4495	2522 (56.1)	2254	1244 (55.2)	0.475
Vitals at Presentation					
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	2254	98.7 (98.1 - 99.8)	<0.001
SBP (IQR) - mmHg	4469	131 (114 - 148)	2254	132 (117 - 148)	0.002
DBP (IQR) - mmHg	4465	75 (65 - 84)	2252	75 (67 - 84)	0.117
HR (IQR) – bpm	4467	98 (85 - 112)	2253	95 (82 - 107)	<0.001

Oxygen saturation (IQR) - %	4463	95 (91 - 98)	2253	96 (92 - 98)	<0.001
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	2254	19 (18 - 22)	<0.001
Laboratory Markers					
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	2228	12.9 (11.5 - 14.2)	0.030
Platelet count (IQR) -k/µL	4372	188 (116 - 260)	2228	196 (143 - 259)	<0.001
White blood cell count (IQR) - k/µL	4372	7.5 (5.6 - 10.6)	2228	6.4 (4.7 - 8.8)	<0.001
Absolute lymphocyte count (IQR) - k/µL	4420	1 (0.7 - 1.4)	2246	1 (0.7 - 1.4)	0.062
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	2253	137 (134 - 140)	<0.001
Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	2243	4.1 (3.8 - 4.5)	<0.001
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	2253	101 (98 - 104)	<0.001
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	2253	24 (21 - 27)	<0.001
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	2253	1.1 (0.8 - 1.5)	<0.001
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	2253	126 (104 - 184)	<0.001
Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	2084	35 (24 - 55)	<0.001
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	2171	26 (17 - 44)	0.292
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	1913	1.9 (1.4 - 2.5)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	1563	341 (254 - 468)	<0.001
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	1957	126 (67 - 282)	<0.001
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	1907	1.2 (0.7 - 2.3)	<0.001
Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	1252	0.1 (0.1 - 0.3)	<0.001
Troponin T* (IQR) - ng/mL	0	NA	2106	0.01 (0.01 - 0.03)	NA
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	0	NA	NA
Interleukin-6 (IQR) – pg/mL	1056	34 (14 - 75)	710	11 (4 - 26)	<0.001
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	1040	536 (434 - 652)	<0.001

Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	1637	510 (230 - 1094)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. * Troponin T was available only until June 2020, Troponin I was available only after June 2020.

Supplemental Table 3 - Initial Laboratory Blood Tests

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
Hemoglobin (IQR) - g/dL	12.8 (11.2 - 14.1)	12.4 (10.7 - 13.9)	13 (11.6 - 14.3)	12.9 (11.5 - 14.2)
Platelet count (IQR) - k/µL	188 (116 - 260)	228 (169 - 300)	200 (144 - 257)	196 (143 - 259)
White blood cell count (IQR) - k/µL	7.5 (5.6 - 10.6)	8 (5.8 - 11)	6.6 (5.1 - 8.9)	6.4 (4.7 - 8.8)
Absolute lymphocyte count (IQR) - k/µL	1 (0.7 - 1.4)	1.2 (0.9 - 1.8)	1.1 (0.8 - 1.5)	1 (0.7 - 1.4)
Sodium (IQR) – mEq/L	137 (134 - 141)	138 (135 - 141)	137 (135 - 140)	137 (134 - 140)
Potassium (IQR) – mEq/L	4.3 (3.9 - 4.8)	4.2 (3.8 - 4.6)	4 (3.8 - 4.4)	4.1 (3.8 - 4.5)
Chloride (IQR) – mEq/L	98 (95 - 103)	103 (100 - 105)	101 (99 - 104)	101 (98 - 104)
Bicarbonates (IQR) – mEq/L	24 (20 - 26)	24 (21 - 27)	25 (22 - 27)	24 (21 - 27)
Creatinine (IQR) - mg/dL	1.1 (0.8 - 2)	1 (0.8 - 1.5)	1 (0.8 - 1.3)	1.1 (0.8 - 1.5)
Glucose (IQR) - mg/dL	134 (108 - 197)	121 (100 - 171)	122 (102 - 173)	126 (104 - 184)
Aspartate aminotransferase (IQR) - U/L	40 (27 - 65)	26 (20 - 38)	31 (21 - 47)	35 (24 - 55)
Alanine aminotransferase (IQR) - U/L	27 (17 - 44)	21 (14 - 32)	25 (16 - 41)	26 (17 - 44)
Lactic acid (IQR) – mmol/L	2.1 (1.6 - 3)	1.9 (1.4 - 2.7)	1.8 (1.3 - 2.5)	1.9 (1.4 - 2.5)
Lactate dehydrogenase (IQR) - mmol/L	384 (285 - 535)	254.5 (196 - 340)	300 (225 - 383)	341 (254 - 468)
Creatine Kinase (IQR) – U/L	168 (83 - 401)	97 (57 - 176)	116 (60 - 213)	126 (67 - 282)
D-dimer (IQR) - µg/mL	1.8 (0.9 - 3.9)	1.1 (0.5 - 2.2)	0.8 (0.5 - 1.6)	1.2 (0.7 - 2.3)
Procalcitonin (IQR) – ng/mL	0.2 (0.1 - 0.9)	0.1 (0.1 - 0.4)	0.1 (0.1 - 0.2)	0.1 (0.1 - 0.3)
Troponin T* (IQR) - ng/mL	NA	0.01 (0.01 - 0.03)	0.01 (0.01 - 0.02)	0.01 (0.01 - 0.03)
Troponin I* (IQR) – ng/mL	0.01 (0.01 - 0.03)	0.01 (0.01 - 0.01)	NA	NA
Interleukin-6 (IQR) – pg/mL	33.6 (13.8 - 75.2)	11.7 (3 - 43.1)	11 (4.7 - 22.2)	10.8 (4.3 - 25.6)
Fibrinogen (IQR) – mg/dL	624 (491 - 750)	448 (370- 583)	540 (436 - 663)	535.5 (434 - 652)

Ferritin (IQR) – ng/mL	716 (335 - 1498)	228 (90 - 562)	364 (166 - 785)	510 (230 - 1094)

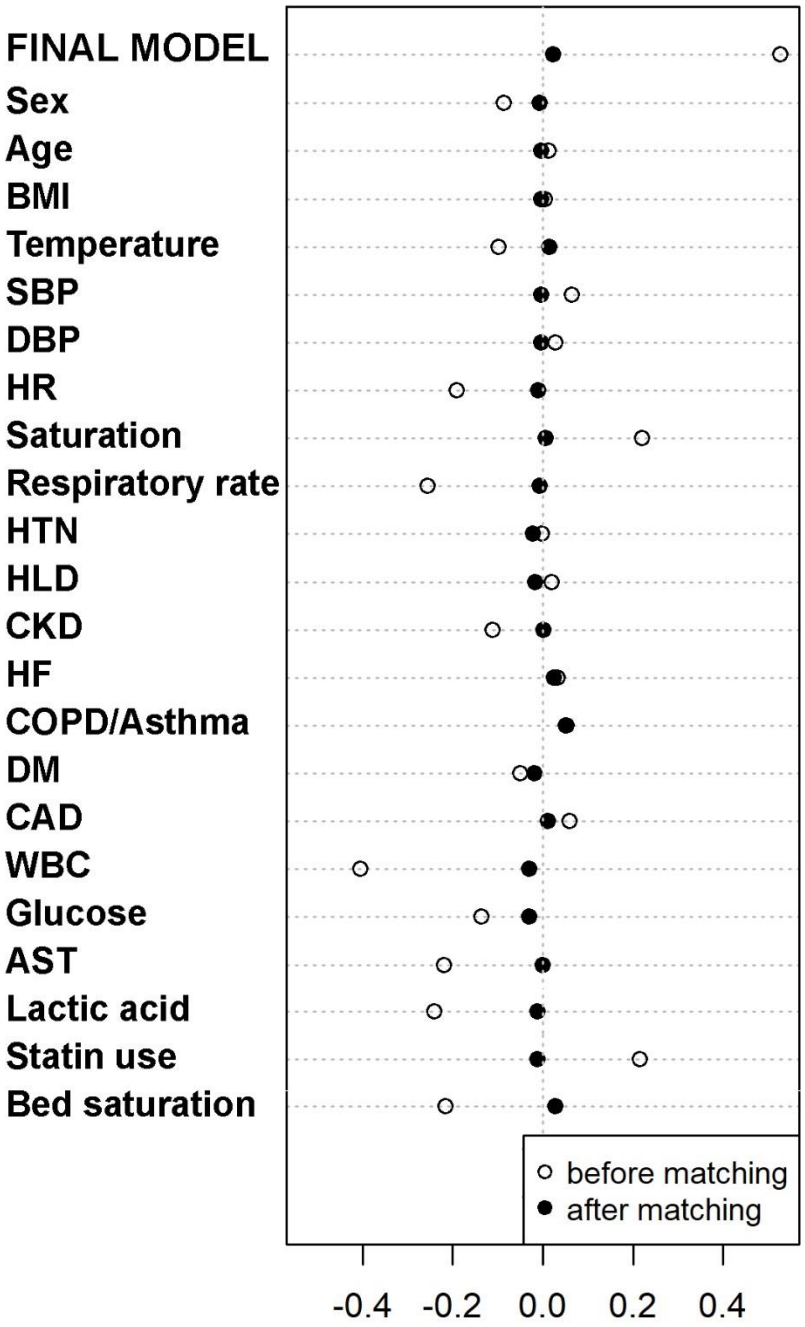
IQR = Interquartile range. * Troponin T was available only until June 2020, Troponin I was available only after June 2020

Supplemental Table 4 - Therapies Administered during the Admission

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
Hydroxychloroquine - no (%)	3007 (66.9)	1 (0.4)	2 (0.5)	8 (0.4)
Azithromycin - no (%)	1322 (29.4)	51 (19.3)	118 (31.3)	374 (16.6)
Other antibiotics - no (%)	3382 (75.2)	160 (60.6)	214 (56.8)	1082 (48)
Steroids - no (%)	1485 (33)	71 (26.9)	195 (51.7)	1462 (64.9)
Angiotensin-converting-enzyme Inhibitors - no (%)	318 (7.1)	36 (13.6)	51 (13.5)	269 (11.9)
Angiotensin II receptor blockers - no (%)	264 (5.9)	23 (8.7)	32 (8.5)	212 (9.4)
Statin - no (%)	1478 (32.9)	109 (41.3)	129 (34.2)	1002 (44.5)
Therapeutic anticoagulation - no (%)	1041/4496 (31.2)	76 (28.8)	98 (26.0)	772 (34.3)
Remdesivir* - no (%)	78 (1.7)	37 (14)	134 (35.5)	1224 (54.3)
Lopinavir/Ritonavir – no (%)	40 (0.9)	0 (0)	0 (0)	0 (0)
Ivermectin – no (%)	11 (0.2)	1 (0.4)	0 (0)	34 (1.5)

* 45 patients listed as remdesivir recipients in the spring season were part of a 1:1 double-blind, placebo-controlled study. Instead, all the patients in summer, fall, and winter seasons listed as remdesivir recipients received the actual medication.

Supplemental Figure 1 - Distribution of Propensity Score



AST = aspartate transaminase; BMI= body mass index; CAD= coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; DBP= diastolic blood pressure; DM = Diabetes mellitus; HF= heart failure; HLD = hyperlipidemia; HNT = hypertension; HR = heart rate; SBP = systolic blood pressure; WBC = white blood cell count

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4-5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 Supp
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12-13
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	Supp
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.